ORIGINA

UNITED STATES OF AMERICA
BEFORE THE FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

In the Matter of:	:	
Enrofloxacin for Poultry: Withdrawal of Approval of Bayer Corporation's New Animal Drug Application (NADA) 140-828 (Baytril)	:	FDA DOCKET NO. 00N-1571

Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland

Wednesday, May 7, 2003

THE HEARING in the above-entitled matter commenced at 9:00 a.m., pursuant to notice.

BEFORE:

DANIEL J. DAVIDSON, Administrative Law Judge

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APPEARANCES:

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Also present:

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C O N T E N T S

P R O C E E D I N G S

JUDGE DAVIDSON: Good morning. Come to order. We'll go off the record for a moment while I get set up here.

(Off the record.)

JUDGE DAVIDSON: Preliminary matters?

MR. KRAUSS: Good morning, your Honor. Gregory Krauss on behalf of Bayer. I have one preliminary matter.

You had asked about whether there was an Exhibit B-1935, and I went back and checked and then recalled that after Dr. Angulo's testimony regarding incidence and confounding, I had copied some pages out of Modern Epidemiology on those topics.

He had said Modern Epidemiology, by Rothman and Greenland, is the book that they use at CDC and that he was most familiar with, so I had copied those pages and forgot to do anything with them until you reminded me about 1935.

At this time, I would like to move into evidence B-1935, which is the cover, certain title pages, and related subject index entries from that book

that relate to incidence and confounding.

JUDGE DAVIDSON: Have you got copies for everybody?

MR. KRAUSS: Excuse me, your Honor?

JUDGE DAVIDSON: Copies for everybody.

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: Including the reporter?

MR. KRAUSS: Yes, your Honor.

MR. SPILLER: The Center does not object, your Honor.

JUDGE DAVIDSON: No objection, then it's moved in. But I want to see it and have it and have the reporter have a copy.

MR. KRAUSS: Yes, your Honor. Thank you, your Honor.

(Respondent Exhibit 1935 was marked for identification and received in evidence.)

JUDGE DAVIDSON: Okay. Mr. Nicholas?

MR. NICHOLAS: Your Honor, I have one preliminary matter as well. Yesterday, Mr. Spiller questioned Dr. Cox about his degrees and background,

and, as a result of that, your Honor, in about 10 minutes we spoke to the Registrar's office at MIT and what I'd like to present to the Court are two things, your Honor.

One is marked B-1946 and it's from the Registrar's office at MIT and it clearly shows that when you get the raw data and you ask the right questions you will get the correct answer. It will show, your Honor --

JUDGE DAVIDSON: Well, that says what it says. Let's move on. Come on.

MR. NICHOLAS: So this is one exhibit. This is 19 --

JUDGE DAVIDSON: 46?

(Respondent Exhibit 1946 was marked for identification.)

MR. NICHOLAS: -- 46, your Honor. And the other exhibit, your HONOR, is the transcript from MIT that clearly shows that Dr. Cox got his B.A. from Harvard -- A.B. from Harvard in 1978 and it's a certified copy of his transcript and I'd like to mark that as 1947.

JUDGE DAVIDSON: Okay. Copies?

MR. NICHOLAS: I might add it also shows that Mr. Cox -- Dr. Cox got primarily A's at MIT.

JUDGE DAVIDSON: Wow. I'm not surprised.

(Respondent Exhibit 1947 was marked for identification.)

JUDGE DAVIDSON: Okay.

MS. STEINBERG: Your Honor, would you like us to respond now to your question on the documents that have been moved into evidence or have been ruled on?

JUDGE DAVIDSON: I'm ready to rule on that part. I was waiting to hear about the -- what I consider the underlying documentation with respect to the FOI which you were supposed to have decided on, but I don't know if I even want to let you at this point. As far as I'm concerned, it's out. All of it.

So if you give me the numbers, I'll mark them out. This is the letters and correspondence dealing with your FOIA request. It stays in the 1285, it becomes a particular issue in the case, you can still refer to it but I don't consider it the quality that I like to have as evidence in my case.

MS. STEINBERG: Your Honor, that would be G-1801, B-1937, and there's a question about the next four, B-1938 through B-1941. These are declarations by two Bayer witnesses and one Bayer employee and one Bayer counsel, and I would like verification of --

JUDGE DAVIDSON: I mean, those, too, if they deal with the FOIA request.

MS. STEINBERG: Yes. B-1940 and B-1941, a declaration by Michael Bond do deal with the FOIA request. B-1938 and B-1939, the declarations from two witnesses go a little bit further and admit to errors in testimony, and we'd like to address that as well, your Honor.

JUDGE DAVIDSON: Address it?

MS. STEINBERG: Well, CVM would like to join, if Bayer is willing to move to withdraw those portions which are admittedly in error, or alternatively, CVM would like to move to strike those portions of the testimony which are admitted in error.

JUDGE DAVIDSON: Well, they're not admitted. Are we talking about previous exhibits?

MS. STEINBERG: In the declarations of Dr.

Burkhardt and Dr. DeGrouth.

JUDGE DAVIDSON: I thought you were supposed to confer on these before this morning?

MS. STEINBERG: We did, your Honor.

JUDGE DAVIDSON: And what did you decide? You couldn't decide?

MS. STEINBERG: Well, we could not reach agreement on this.

MR. NICHOLAS: Your Honor, if I may, with respect to those two declarations, I think it's important for the Court to understand the circumstances under which that testimony was presented, based upon data that was supplied by CDC.

JUDGE DAVIDSON: I got it. I'm sorry. It's not your fault. It's mine. I don't understand when you say testimony. You're talking about other exhibits testimony as opposed to these declarations.

MR. NICHOLAS: The declarations by Dr. Burkhardt and Dr. DeGrouth are in part withdrawing part of their written direct testimony which was submitted in December. What was contained in their written direct testimony in December was in part based upon

inaccurate information that was provided to Bayer by the Centers for Disease Control.

So upon review of the two data sets, we determined, or the witnesses determined, that certain minor portions of their testimony were inaccurate and therefore should be withdrawn, and we put those in the declarations as a way of explaining the circumstances rather than dealing with withdrawing their testimony. And one of the witnesses, I believe, although perhaps both, has stated that these changes do not affect generally the conclusions they reached in the testimony.

MS. STEINBERG: Your Honor, one additional thing, if I may. Dr. DeGrouth seems to change part of his testimony in that declaration, and I just want to be on record saying CVM would oppose any change to written direct testimony at this late date --

JUDGE DAVIDSON: When you say change, you mean an addition?

MS. STEINBERG: A substitution, withdrawing part of it and substituting --

JUDGE DAVIDSON: And adding something else.

MS. STEINBERG: Yes.

JUDGE DAVIDSON: Well, it's not -- none of the exhibits are received, but I do require that for the record, probably you, Mr. Nicholas, submit something to the record indicating what portions of the testimony are being withdrawn, solely what's being withdrawn.

MR. NICHOLAS: Yes, your Honor.

JUDGE DAVIDSON: Okay?

MR. NICHOLAS: Thank you, your Honor.

JUDGE DAVIDSON: Because that has to be indicated on the record so we know what is in and what is out when we review the testimony of those witnesses.

MR. NICHOLAS: Certainly, your Honor. I would request that we are able to represent the circumstances under which it's withdrawn, your Honor.

JUDGE DAVIDSON: Well, I think you did that. Didn't you just do that?

MR. NICHOLAS: Well, I did, but as I understand it, none of these documents are in evidence, so --

JUDGE DAVIDSON: Doesn't matter. They're on the record as far as -- I mean, you can refer to them

all you want as long as you point out that I don't consider them evidence, but say that's your representation of what happened. So you want to represent it again?

MR. NICHOLAS: No, I'm fine, your Honor. Thank you.

JUDGE DAVIDSON: Okay. Let's see. Before I rule on your motion to add two exhibits and -- I think we've already let the others in -- I have some problems with our record.

First of all, apparently on December 20, 2002, a motion was filed which was unopposed, so it's not a problem, except that I never got a copy of it. Maybe that was one of those phantom faxes that you sent me. I think I know what happened. At one point your office was sending me faxes through my telephone number and I don't get them through my telephone number. I did call and straighten that out with one of your assistants.

But it's not important except for the fact that the record doesn't reflect these exhibits being moved -- being accepted in evidence. They were unopposed. So, for the record, Exhibits B-273 through

280, are now received in evidence, since that motion, which I know I have a copy of, says that it was unopposed.

MR. NICHOLAS: Thank you, your Honor.

(Respondent Exhibits 273 through 280 were marked for identification and received in evidence.)

JUDGE DAVIDSON: Now, yesterday during the cross-examination I was referred to Exhibit B-122, Exhibit B-295, and Exhibit B-1573 and Exhibit B-1886, with the representation that they were part of the record. They're not. They were never moved into evidence, as far as my records show. There may be others.

And at this point, while Mr. Spiller is looking to see what the problem is and straighten me out -- I'm sure he will -- if I said anything on the record that was in any way derogatory of our dockets management branch for not providing me with the right information, I have to apologize profusely and indicate that Mr. Lyle Jaffe has done a wonderful job of keeping

up with the record and what's going on and what's not going on, for the record.

He straightened me out with this one very quickly.

MR. SPILLER: Your Honor, I apologize for my misunderstanding which I presented to the record yesterday, that each of those Bayer exhibits was in the record.

The clearest of those I think is B-1573, which I believe is Dr. Cox's biographical sketch, which I believe both sides would probably want to be in the record, but I should ask explicitly of Mr. Nicholas if I have that right.

Did you intend for his biographical sketch to be presented to the record?

MR. NICHOLAS: We have no objection to it being in the record.

MR. SPILLER: And the Center concurs with that -- does not object to that, your Honor.

JUDGE DAVIDSON: All right. B-1573 is in the record.

(Respondent Exhibit 1573 was marked for identification and received in evidence.)

MR. SPILLER: B-1886, I believe, is the Rodriguez article that is cited numerous times, and testimony yesterday includes the reference that it was cited numerous times in Dr. Cox's testimony. I had thought that Bayer had moved it in. I was evidently mistaken. The Center moves now for the admission of the Rodriguez paper, B-1886.

MR. NICHOLAS: If I may, your Honor, that document is in evidence. It's G-1711, I believe.

JUDGE DAVIDSON: Ah-ha. That's the problem.

MR. SPILLER: Thank you, Mr. Nicholas.

JUDGE DAVIDSON: So we don't have to do anything with that. That's G -- say that again.

MR. NICHOLAS: 1711, your Honor.

JUDGE DAVIDSON: Okay.

MR. SPILLER: And that may or may not be the case with Exhibits B-295 and B-122 which we referred to already, as your Honor pointed out, in yesterday's testimony. B-122 is the Adak paper, I believe, and B-

295 is Eberhart Phillips, which is also cited in Dr. Cox's testimony.

MR. NICHOLAS: Those are both in evidence, your Honor, with G numbers.

JUDGE DAVIDSON: Furnish them, please.

MR. SPILLER: Under the principle of countervailing blunders, I was accidentally right, because they were other exhibits.

JUDGE DAVIDSON: I thought you would straighten me out, as I said.

MR. SPILLER: Thank you, your Honor.

JUDGE DAVIDSON: Now, I've reviewed B-1924 through 27; have been received in evidence. The only remaining ones I have to deal with are B-1923 and 1928. I'm having a big problem because, well, this agency doesn't provide, as many others do, for closing the record at a particular time. At some point in time it's got to close. And as far as I'm concerned, this is as good as any, because after this, there's no possibility of cross-examination, so I can't accept new stuff.

So I'm not going to accept those two exhibits

because they do include material which I find is additional and not the same as what was in before, when the Center had an opportunity to request cross-examination from those witnesses.

So 1923 and 1928 are not received in evidence, and I don't want to see any more evidence moved in unless it falls strictly under the very concise -- my own very concise guidelines for what constitutes "new" evidence.

In other words, if it's of such moment that I have to consider it before I can make a decision, because it affects the total outcome of the case and it has truly not been available prior to the time it's submitted, then I will consider it as new evidence and I will rule on whether I will accept it or not, even if it means delaying the proceeding, but it's got to be something really blockbuster size, otherwise I don't want any more exhibits that are trying to put evidence in the record or testimony, as of right this second.

Now, are there -- let's see. B-1946, and there was another one?

MR. NICHOLAS: 1947, your Honor, which was Dr.

Cox's --

JUDGE DAVIDSON: 1947. Was there an objection to that?

MR. SPILLER: No, your Honor. There is not an objection. I had thought that these documents would come in as a part of the redirect, but I'm happy to respond now.

I'd note that B-1946, although it's addressed to a different person, is the same information that we presented yesterday, and one of the reasons we would not object to its admission is that it also reflects that it's a Doctor of Philosophy and it does not specify risk analysis. Neither do the attached documents.

We do not object to B-1947. It also reflects an admirable great record and unless I have missed something here, also does not specify that the Ph.D. was awarded in risk analysis. It does -- one of them -- I think the commencement program does specify the thesis in the field of risk analysis and, as the witness' testimony yesterday indicated, the thesis was in risk measurement, which, as he testified, is a

subset of risk analysis.

JUDGE DAVIDSON: Do you want to say something?

MR. NICHOLAS: No, your Honor. I think there's no reason to belabor the point. I think it's obvious that Dr. Cox is an expert in this field and --

JUDGE DAVIDSON: Okay. They are in evidence. I haven't yet heard a challenge to that.

(Respondent Exhibits 1946 and 1947 were received in evidence.)

JUDGE DAVIDSON: That's it?

Okay. Dr. Cox, I think we're ready for you to resume your second favorite seat.

THE WITNESS: Thank you, sir.

JUDGE DAVIDSON: Let the record reflect that Dr. Cox is still under oath.

MR. NICHOLAS: Your Honor, I'd like to approach the witness and give him a copy of --

JUDGE DAVIDSON: Go ahead.

Whereupon,

LOUIE COX, JR.

was recalled as a witness and, having previously been duly sworn, was examined and testified further as follows:

REDIRECT EXAMINATION

BY MR. NICHOLAS:

Q And would you just identify that for the record, please, Dr. Cox, by the exhibit number?

A It's Exhibit number B-1901.

Q And that's a copy of your testimony. Is that correct?

A Yes. This appears to be a copy of my written direct testimony.

Q And the signature page, on page 8, I believe, is that your signature?

A Yes. It is.

Q Thank you.

A Thank you.

RECROSS EXAMINATION

BY MR. SPILLER:

Q Dr. Cox, in the document that Bayer's counsel just provided for you, B-1901, would you open that to page 16, please?

A Okay.

Q That's one of the many pages where you cited the Rosenquist, et al. article in the large paragraph

at the bottom of the page.

A Yes.

Q Based on Rosenquist at that point, your view that CVM model assumption of a linear relationship between exposure to contaminated chicken and the number of human campylobacteriosis cases is false. Is that right?

A Can you -- there are several things here. I don't see those exact words.

Q And exact words are important, aren't they? So I should get that right.

A Please.

Q In the sixth line of that large paragraph at the bottom, beginning with the word lacking --

A Yes.

Q -- I won't read it out loud, do you argue that the CVM model cannot correctly estimate the loads of people, and you cite Rosenquist?

A I do say that it cannot correctly estimate the risks from the microbial loads of campylobacter, yes.

Q And in the next sentence you say that the CVM model incorrectly assumes the risk is proportional to

the prevalence of contaminated chicken servings ingested.

A Yes, rather than recognizing it was disproportionately caused -- yes.

Q When you actually referred, though, to the CVM model, did you find that the CVM model was based on chicken servings or to the overall consumption of chicken?

A If I recall correctly, I think it's --

MR. NICHOLAS: Excuse me, your Honor. If the witness could be provided with a copy of the risk assessment, so he could have that document to review.

THE WITNESS: Oh, thank you. And perhaps the Rosenquist paper?

BY MR. SPILLER:

Q We'll get to the Rosenquist paper and I'll certainly provide you with a copy of the FDA's risk assessment. But I would like to ask your recollection of that.

Do you believe that the FDA risk assessment actually relied on servings?

A No, I don't think that it did.

Q I'm giving you now a copy of the FDA risk assessment, G-953.

A Thanks. I think you're -- perhaps you could restate your question. I'll try to give you a straight answer.

Q Your quote beginning on the ninth line of the largest bottom paragraph on page 16, the sentence beginning, instead, it incorrectly assumes, continues that risk is proportional to prevalence of contaminated chicken servings ingested.

And the question is whether or not you have accurately attributed the term servings to FDA or isn't that your insert instead.

A Oh. Well, as you know, if several quantities are all proportional to each other, then something that's proportional to one is proportional to all, although with different constant in proportionality.

I believe, although in 5 -- 6 or -- I don't remember where this is -- I have a hard time finding it -- I believe that CVM said that risk is proportional to exposure and in some places, I believe treated exposure in terms of pounds of contaminated chicken at the

reduction stage.

And I believe that then consumption, servings, if there are four servings per unit, other things that are proportional to pounds of contaminated chicken would also be proportional to risk.

Q I appreciate hearing your belief. Am I correct that you confirmed that the FDA risk estimate refers to pounds of chicken produced and not to servings ingested?

A Without taking the time to re-read this document, I believe that it refers in some places, certainly to servings. I believe that it refers in defining exposure to pounds of contaminated chicken. I'm almost sure that that's at a point of production.

So I think there are different exposure measures.

Q At any rate, at several places in the paper, and we can go through them if we need to, but am I correct that you have complained of FDA's assertion of a linear relationship between the contaminated chicken and the illness in humans at a number of places in your testimony?

A That is correct.

Q And among the support you cite for that is the Rosenquist 2000, and counsel has provided that I provide you a copy of that. I'm happy to.

A Thank you.

Q Counsel still has the copy that I provided him yesterday. That Rosenquist article is Exhibit G-1788.

MR. SPILLER: And, your Honor, I believe I provided that yesterday.

BY MR. SPILLER:

Q And you quote that on the same page 16 of your testimony, don't you, Dr. Cox, about 7 lines up from the bottom of the page, the lines begins with the word invalidates. Do you see a sentence that begins as stated by Rosenquist, et al., ibid. You see that?

A I do.

Q And the ibid is in the same place, am I roughly right on the Latin, and so that is a back reference to the next previous cite to Rosenquist, et al., section 7.2.2. Am I right?

A That's correct.

Q And that's found, isn't it, on page 10 of

Exhibit G-1788?

A Yes, it is.

Q Well, go with me there and see if you can help me figure out how you got that quote.

A Uh-huh.

Q Your quote begins the minor effect. Am I right?

A Yes.

Q And that language occurs on the fourth line from the bottom of that page.

A Uh-huh.

Q And for convenience, and not to introduce an additional exhibit, I have a blowup of that page of the testimony. Unfortunately I don't have -- this is --

MR. NICHOLAS: Your Honor, I believe that's a blowup of the article. I believe counsel said it was a blowup of the testimony.

MR. SPILLER: I apologize. Counsel is correct. This is a blowup of one page of G-1788, page 10.

BY MR. SPILLER:

Q And you can refer to whichever you want to,

Dr. Cox. And what we're talking about is down at the bottom of the page where it says the minor. That's where your quote begins. And then as I try to read along, why don't you read your quote, and I want to follow along here.

A Okay. Do you want my interlineations or --

Q Yes, please, and I'll write them in here and we'll see how you constructed that.

A Okay. The minor effect, then my interpolation, less than 10 percent reduction --

Q All right. Pause there. Less than 10 percent reduction. And you fairly show that in the box brackets.

A Yes. And it's from six lines above.

Q Okay.

A It's in the same paragraph.

Q Right.

A On the number of, then my interpolation, CP standing for campylobacter --

Q And that's fair. You put that in box brackets, so we'll tuck that in.

A -- the number of positive carcasses at the end

of slaughter, even after introduction of a decrease of three log units -- and I said three log 10 units, although I see in this version of the article it just says three log units.

Q I'll write in 10.

A Okay. Demonstrate the need --

Q Do you have an S after the word "demonstrate"?

A Yes.

Q So we'll add that. That wasn't single, but that's a small thing, so we'll add that here. Demonstrates.

A You're right. Of course, minor effect demonstrates.

Q All right. That's a grammatical correction that you made. Go ahead.

A Demonstrates the need for quantitative detection methods.

Q Okay.

A Comma, then there's my ellipsis -- shall I keep reading?

Q After methods, do you have a period?

A Yes, I have a period with an ellipsis.

Q Okay. A period. So you ended the sentence there and then an ellipsis. Go ahead.

A Okay. Continuing to read from Rosenquist, as the effect of such a decrease --

Q Okay. I need you to pause here for just a minute. I'm off the end of my observed territory. We may have a discrepancy. There's a phrase in your testimony, Dr. Cox, that I don't think you mentioned here. Do you have a relatively large reduction in the number of campylobacter on the chickens, for example -- that's in your testimony, right?

A Yes, I see that. Yes.

Q Yes. I see that. And that's not in the quote there, is it? In the original.

A Are you ask -- let me see.

Q Now I don't want to be unfair to you, Dr. Cox. I think I know where that came from. I think it came from up higher in the paragraph, on the first line there, relatively large. Do you think that's where it came from?

A Well, now -- hold on a second. I was so busy reading for you from the Rosenquist paper that I --

Q I'm sorry. I wanted you to be reading to me from your purported quote of the Rosenquist --

A Thank you, yes. The minor effect -- okay. Now I'm back on track. On the number of CP positive carcasses. Right. At the end of slaughter, even after -- you know, I think this is from the -- must be from the final published form of the paper that I've quoted here. And I see that you're quoting from the -- well, article in press shouldn't be different.

Q Would you like to find that article?

A Yes, I think it might be helpful.

Q Is that in the record?

A I don't know. I do recognize from the stamp article in press and the XXXXX at the top of the page and so forth. These may be galleys. And I know what I looked at in preparing this.

Q So you're sure you got that from the actual published article.

A A copy of the published article, yes.

MR. SPILLER: Sorry, your Honor. I don't have multiple copies of this. It's not in the record, but --

BY MR. SPILLER:

Q Dr. Cox --

JUDGE DAVIDSON: Let's handle it this way. We'll go off the record and you can show him what you're talking about and if there's agreement, we'll go back on the record and you tell me what it is. If there's a disagreement, we'll go back on the record and you can each tell me what it is.

MR. SPILLER: Thank you, your Honor.

JUDGE DAVIDSON: Off the record.

(A discussion was held off the record.)

JUDGE DAVIDSON: On the record.

MR. SPILLER: Thank you, your Honor.

BY MR. SPILLER:

Q Now, Dr. Cox, have you and I just, with the assistance of Bayer's counsel, compared the published version of this article to the in press version, which is the exhibit?

A Yes, we have.

Q And have we found that the words are the same and in the same order in the -- for this relevant paragraph for the published version to which you had

thought you were referring?

A Yes, they are.

Q Continuing, then, with our investigation of how this quote was assembled, in your quote, after the word "slaughter" in the exhibit, have you inserted the word "of" in box brackets?

A Yes.

Q And then after that, have you inserted another ellipsis?

A The first ellipsis, yes.

Q And after that, did you move some text from higher in that paragraph?

A I quoted text from higher in the paragraph, yes.

Q And where is the beginning of that material?

A Well, as you can see, on the top line under section 7.2.2, the authors interpret what they're doing in the following words: "A relatively large reduction of the number of campylobacter on the chickens."

Q So the portion that you moved down there begins with "a relatively"?

A Yes. A relatively large reduction in the

number of campylobacter on the chickens, and they --

Q How large a bubble did you take of the text there?

A I continued through, for example -- oh, here's where the log 10 comes in. For example, a reduction of three log 10 colony forming units per chicken. So that would be a thousandfold reduction is what they're talking about.

Q Down through the word "chicken," is that how far that bubble extends?

A CFU/chicken, yes.

Q All right. That comes down to here. And then you stitch that in after the ellipsis?

A I quoted it between the ellipses, yes.

Q And then the text continues in the actual paper that you're including in these quotes, even after introduction, but your ellipses covered that. So we struck some words out there. We struck out even after introduction of a decrease of three log units?

A Yes. I think that's right. Uh-huh. Yeah.

Q And then it continues, "demonstrate," you added the S, "for quantitative detection methods" and

you put in a period there. And then we struck the last four words out of that line, right?

A As the effect of.

Q Okay. So then we go -- and for convenience I have a blowup of that segment from your testimony to 16, and here is another copy of the next page of Exhibit G-1788, and it's exhibit page 11 now.

And on that page, the deletion continues through the first two lines. That comes out and then an ellipsis, right, before the "the"?

A Well, yes. What I show is not a quote but which is pertinent and reflects the point there is that the effect of such a decrease in the number -- it's a pretty large decrease in the number of campylobacter would not have been detected by the -- what he refers to as "qualitative methods," meaning the prevalence metric.

Q So did I understand your testimony correctly, you agree that's pertinent and you chose not to quote it?

A You give part of what I said. It's pertinent. It agrees fully with and is covered by what he has

said, and I chose not to belabor it, yes.

Q And then you continued, referring to your quote now, "with the incidence of campylobacteriosis related to consumption of" -- he said "a chicken meal" but you deleted "a" and "meal," didn't you?

A It sure looks that way, but could you just hand me the final article one more time? We don't need to go off and on. I just want to --

Q It's up to the Court whether we go off and on. I'm willing to hand you the published article. I'm handing you now -- excuse me. I've got to get you that published article.

MR. NICHOLAS: Your Honor, if I may, we would have no objection to moving the final article into evidence. CVM's counsel would as well. It just seems to me it would make this -- would facilitate this and make it easier rather than going back and forth.

JUDGE DAVIDSON: I don't know what's in the final article, so -- I don't know how it differs, if it does, what's the difference between the final and this.

MR. NICHOLAS: I don't know. That's why I was suggesting --

JUDGE DAVIDSON: Thank you. We'll see what goes on.

BY MR. SPILLER:

Q Dr. Cox, do you have before you now the final published article?

A I do.

Q And it also says a chicken meal, doesn't it?

A Yes, it does, not --

Q But you didn't say that in your quote, did you?

A I said consumption of chicken, not consumption of a chicken meal. Thank you. Was reduced significantly. Yes. Okay.

Q And then continuing, your quote has a comma after the word "carcasses," not in the original, and you deleted references to figure 7(c) --

MR. NICHOLAS: Excuse me, your Honor. Your Honor, I'm unsure where counsel is. I'm --

MR. SPILLER: I'm on -- I'm sorry, your Honor.

MR. NICHOLAS: -- excuse me. He's referencing Dr. Cox's quote as though he's quoting from the article and as I see Dr. Cox's testimony, it appears the quote,

in this paragraph, at least, appears to end at the top of page 17, first line, where it says "positive chickens." So I'm a little confused.

JUDGE DAVIDSON: Well, he's still on the bottom of page 16.

MR. NICHOLAS: Thank you, your Honor.

MR. SPILLER: Mr. Nicholas makes strong points, your Honor. This is a quote and we're continuing to work with the quote and to compare it to the text from which it was allegedly taken.

THE WITNESS: Okay. So where's the comma that shouldn't be there?

JUDGE DAVIDSON: Last line on your page 16.

THE WITNESS: I see that.

BY MR. SPILLER:

Q And the original refers, am I correct, Dr. Cox --

A Reduce the number of -- on the carcasses, comma -- yes, yes, yes. This is -- yes. I see. Because he's referring to a figure 7(c) and there is no figure 7(c) in my --

Q And he has a period which you've deleted, so

you've run the sentence on. So we'll make it a lower case E for the "even." Isn't that what you did?

A I deleted the reference to figure 7(c) since I'm not copying or referring to figure 7(c).

Q And I hope we will later but let's see, then. He ended the sentence but you didn't. You make the quote with the small E in the word "even" there, right?

A Uh-huh. Yes.

Q And then --

A Okay.

Q -- we also delete after the word "positive" chickens the entire rest of -- you had the thing ending after "the number of campylobacter on the positive chickens." Is that right? Here? Excuse me. When I say here, the next to bottom line on Exhibit G-1788, page 11.

A Yes.

Q Okay. So we put a period there and we actually delete not only 7(a) but the rest of that sentence, because his period is not until here.

A Right. Figure 7(c) and figure 7(a) have been deleted and only his words remain. That's true. With

a sentence break change. That's correct. And in fact -- yes. The sentence you just referred to, "even though such a reduction had almost no influence on the fraction of positive chickens," let me go back to my ellipses, "a relatively large reduction in the number of campylobacter on chickens."

Yes, it was already covered in the preceding ellipses.

Q And to summarize, Dr. Cox, for illustration purposes, I'm showing you what has been marked and is not yet in evidence as G-1813.

MR. SPILLER: I'll give one to the Court, one to the reporter, and one to counsel.

BY MR. SPILLER:

Q I'll be quiet for a moment, Dr. Cox. Would you look that over and see if that summarizes the markups you needed to make to convert what that article said to the quote that you used in your testimony?

(The witness examined the document.)

A It does not.

Q All right. Let's describe -- would you describe anything that shows on that G-1813 that is not

something that was done to convert what the article said with what you quoted?

A Yes. First, I think you'll see that the quoted extract represents using Rosenquist, et al.'s words, the meaning, the essential content of what they've said here.

Q Yes. Indeed, in your testimony, you said Rosenquist -- as stated by Rosenquist -- I'm reading from your testimony on page 16. So you not only quoted, you attributed to them, "as stated by."

A Yes.

Q Okay. We agree on that.

A Now, you've crossed out in what you've just handed me several things that seem to me to be relevant. One is the less than 10 percent, which I had put in square brackets, less than 10 percent reduction.

Q And that's shown on this copy, isn't it?

A Well, with a big X through it. I take it -- you see there's one big X in what you just handed to me?

Q I do.

A You'll see that less than 10 percent, in

parentheses, in the line that starts with that "less than 10 percent" in parentheses, I take it that the X is supposed to strike that entire passage. Is that right?

Q So that could be reflected, instead of the box bracket, as a bubble of moved text, couldn't it?

A Yes. I inserted the word "reduction" for clarity so it's not it exactly, but yes, I mean, we're -- it could have been.

Then you struck out "on the contrary, the number of campylobacter on the positive chickens was significantly reduced," figure 7(b), which, of course, I don't refer to the figure.

JUDGE DAVIDSON: All right. Let's stop for a second.

THE WITNESS: Okay.

JUDGE DAVIDSON: Why don't you go through it again? Remember what the question was.

THE WITNESS: He said what are the differences.

JUDGE DAVIDSON: No, no. He asked you if that adequately reflected your testimony, as it changed the

actual language of the Rosenquist exhibit.

THE WITNESS: Thank you, your Honor.

JUDGE DAVIDSON: You started off by saying no, because you've got the main -- you meant everything that's in there, you covered -- but that's not what the question was.

THE WITNESS: I just said because he nuked this out.

JUDGE DAVIDSON: You can note what you want. I'm going to allow you time to look at it and decide whether or not that accurately reflects what you just testified to as far as differences between your testimony, the quote, and the material in the exhibit.

THE WITNESS: Thank you, your Honor.

JUDGE DAVIDSON: Okay. Off the record.

(Off the record.)

JUDGE DAVIDSON: I wasn't eavesdropping, but I couldn't help hearing what you were talking about and I guess the answer is the record will speak for itself. We have everything in here.

We have -- and you'll correct me if I'm wrong, Dr. Cox. Your position is even though the quote is

inaccurate as a quote, it doesn't change the meaning of what you meant to say.

THE WITNESS: Yes, your Honor.

JUDGE DAVIDSON: Okay.

Move on, please.

MR. SPILLER: Your Honor, may I preserve this by moving in evidence what's been marked as G-1813 as an indication of the difference between that which was quoted from and the quote that appeared?

JUDGE DAVIDSON: No, not this way, because we've got your scratching on there, which the witness seems reluctant to accept, although the record does speak for itself. If you want to put in a copy -- is G-1813 in the record already without your markings on it?

MR. SPILLER: Yes, your Honor. It is a part of G-1788 as reflected on that page. It's page 10 there.

JUDGE DAVIDSON: Page 10 of 1788. Well, it's already in the record, so I won't receive 1813, because I can't get agreement from this side, but I can figure it out myself whether I like your hand scratching or not.

MR. SPILLER: Thank you, your Honor.

BY MR. SPILLER:

Q And Dr. Cox, after all of this, did the process that you followed in determining how to quote this accord with your typical standards for the process of quoting scientific work?

A In the process of trying to give sufficient information for you to find a cite, read it yourself, see if what I said is correct, which is -- let me back up. This is not -- the deletion of figure -- there are several things on here. The deletions of references to the figure --

JUDGE DAVIDSON: Excuse me, Doctor. I think you've already explained what's going on. You've already explained that it doesn't change your testimony or the import of it, so you don't have to go into that again.

THE WITNESS: Right. But he's saying --

JUDGE DAVIDSON: The question was -- the question was is this the way you quote scientific articles.

THE WITNESS: Right.

JUDGE DAVIDSON: And the answer is either yes or no, and then you can explain.

THE WITNESS: Your Honor, I was just about to give, I hope, a responsive answer. How I quote scientific articles depends on the purpose and context of the quote. In all of the cases, if I'm not referring to figures, specialized to the context such as 7(a) and 7(b) and something that I pull out, or if a reference, for example, a number is given, reference 17, that's not pertinent to the content, I would not feel obliged to repeat those typographical marks in the quoted section -- for example, in a journal article.

However, in a journal article, I would try to quote in extenso, if necessary, to get the whole thing in, leaving out only the figure 7(a), figure 7(b), perhaps numbered references that wouldn't mean anything in the context of my quote.

In this context of giving my direct testimony, my emphasis was on finding the supporting quote and giving it in enough detail and adequate citation so that everyone could see what I was talking about. And so that's a somewhat different context from a journal

article, for example.

BY MR. SPILLER:

Q I'll ask a slightly different question. Dr. Cox, for the purpose of your sworn, ratified, written direct testimony in an administrative hearing before the Food and Drug Administration, do you consider this to be an example of a fair quote from you?

A I think that correcting the punctuation and putting in the S -- I think that's fair. The how to deal with the sentence break around the deleted figure reference, in light of our long discussion, I question in my own mind whether it would have been useful to have quoted the entire thing either though that would be duplicating material already in there.

Substantially, I believe this is a fair quote. I don't think anything is misrepresented that he said and I think it's an important and pertinent point.

Q So as we look at all of your quotes -- and I promise the record I will not do this with all of them -- we should expect this same standard to have been followed throughout your testimony.

MR. NICHOLAS: Asked and answered, your Honor.

THE WITNESS: You can expect -- check them out.

BY MR. SPILLER:

Q I think that teaches us what we need to know, Dr. Cox. Thank you.

A Uh-huh.

Q In that original text, among the omitted text are the very first four words of paragraph 7.2.2 revealing that all of this is derived from a simulation, isn't it?

A Well, actually, it looks to me that this is derived from several simulations.

Q And simulations isn't revealed in your version of the quote, is it?

A There's a lot of stuff that's in the Rosenquist article that I didn't quote, yes. Only the pertinent parts are here.

JUDGE DAVIDSON: I think the question was in your version of the quote -- now, if we have to say the quote referred to on page 10, then we will, but your answer dealt with the entire article, and that wasn't the question.

THE WITNESS: I'm sorry, your Honor. I'll try to be more responsive.

JUDGE DAVIDSON: Thank you.

THE WITNESS: No, I did not repeat that this was a simulation model.

BY MR. SPILLER:

Q You not only didn't repeat it, you didn't say it the first time, did you?

A I'm not sure what the first time is. I pointed out I quoted Rosenquist. Many times I've certainly cited it as an example as a form for simulation model and I presume some familiarity with the -- with what's gone before.

Q So the linear relationship that Rosenquist referred to in another part of that same article, you contend that FDA is in error in depositing a linear relationship between the flat prevalence and the fraction of positive chickens, right? Excuse me. The flat prevalence and the incidence of campylobacteriosis in humans.

A That's importantly incorrect. The linear relationship -- the relationship that I claim is not

linear and that Rosenquist demonstrates is not linear is between microbial load on chicken, not prevalence. And this is a crucial distinction because it's microbial lode and microbial load only that caused campylobacteriosis. This is the relevant exposure metric.

If Enrofloxacin is used or is not used, it changes microbial load. Now, he subsequently did a calculation about prevalence, which is a different concept. Prevalence says not how many microbes is this chicken carrying; prevalence says what fraction of flocks in this case have at least some campylobacter present.

And to me it's fundamental that we can predict risk from microbial load. We cannot predict risk from prevalence, as Rosenquist so nicely shows.

Q Well, let's see what Rosenquist so nicely shows. On page 10 of G-1788, in the left-hand column, the first complete paragraph, Rosenquist says, doesn't she, that the flock prevalence is 1 to 1 relationship. That's linear, right?

A Actually, no. Unfortunately, any shape is 1

to 1; but she does mean any -- I was wrong there, not any shape, but a great many shapes are also 1 to 1. She means a direct proportional relationship.

Q She means linear, doesn't she?

A She means linear, and not only linear, but direct proportion. But notice she's not changing microbial load.

Q Yes, I do notice that. She says that there is a 1 to 1 relationship, direct proportional, as you have described, between the two parameters. And the two parameters she's talking about is flock prevalence and human campylobacteriosis cases, right? That's flock prevalence of campylobacter on the chickens.

A This is -- as you read the article, you'll notice this is specifically in simulation runs where the microbial load has held constant. So, for example, it would be irrelevant to any situation that changed microbial load, such as all the situations I'm looking at where Enrofloxacin use is contemplated.

Q And the linear relationship between flock prevalence for campylobacter contaminated chicken to human campylobacteriosis cases is an ingredient of the

FDA risk assessment model, isn't it?

A No. You're taking this completely out of context, I believe. Her claim is that if you double the proportion of flocks that have some campylobacter in them, so they'd be called campylobacter-positive flocks, and if you leave microbial load in those flocks unchanged, so basically you have twice as many flocks as you did before and they're identical in terms of microbial load distribution as what you had before, then you've in essence doubled the size of your problem and you should expect to double the number of illnesses, all else being constant.

Now, in the CVM risk model there is no choice but to leave all else constant. In the Rosenquist model, as this exhibit that you're helpfully putting up shows, a 10 percent change in microbial load leads to a 30-fold change in illness rates, which is extremely non-linear. And the reason is that in this model, as it should be, it's only the high microbial loads that are causing illnesses.

So for you to say that CVM incorporates an important component is to leave out everything

important which is in simulation runs where microbial load doesn't change, for example, because there's no manipulation of Enrofloxacin use.

Q So referring to G-1788 at page 11 and graphs that you just mentioned, in figure 6(c), that depicts, does it not, flock prevalence compared to the number of human cases per 100,000 population, and we're talking about cases of campylobacteriosis, right?

A It refers to -- if you read the legend you'll see where it refers to simulation sampling points around the fitted line. So it refers to it for specific simulation scenarios that do not include change in microbial load.

The changes in microbial load are described in 7.2.2 in the passage that we so artistically deconstructed.

Q If I ask you about changes in microbial load I hope you'll answer that. Until then, would you let your counsel ask you the questions about microbial load.

A Yes, but you asked whether this is what CVM -- whether this component was also an important component

of CVM's risk assessment, and the answer is no. CVM goes far beyond what Rosenquist has done. You're taking an implicit, and in some places explicit, assumption of Rosenquist and extrapolating it to an entire model as if to say microbial loads can never change.

That's what's in the CVM model.

Q Dr. Cox, would you listen carefully in the next question for the terms microbial load or FDA model?

A I will do so, yes.

Q In Rosenquist G-1788, page 11, figure 6, am I right that figure 6(a) depicts a linear relationship between flock prevalence and fraction of campylobacter positive chickens at the end of slaughter?

A For the simulation runs, yes.

Q And similarly, in that same figure, figure 6(c) depicts a linear relationship between flock prevalence and number of human cases per 100,000 population.

A An approximately linear relationship for these simulations. The reason I'm saying that is it's not a

general relationship. It's a relationship conditioned on what we just talked about, which is holding microbial load constant.

Q And in the bounds discussed in this paper, if among three relationships A's relationship to B is linear and if B's relationship to C is linear, isn't it true that A is linearly related to C?

A Actually, not necessarily, but you're falling into I think just the perhaps confusion that I was trying to clarify which is these are not general relationships. These are plots of perhaps 8 different simulation run outputs.

To that, you're trying to attach a general rule which is that human illness is proportional to flock prevalence. I'm telling you that general rule is an incorrect generalization because in general, microbial loads are not held constant as they are in these simulations.

Q And does Rosenquist use a microbial load distribution?

A Yes, she does, as in the famous paragraph.

Q And does Rosenquist have a dose response model

in this paper?

A Rosenquist uses a dose response model, yes.

Q And yet they have the same linear relationship as the CVM model?

A Absolutely not. I mean, look at this paragraph that we just spent half an hour on. It says a 10 percent change in microbial load leads to a 30-fold change in human illness. That's about as non-linear as you can get. Three log units.

Q And in the CVM risk assessment, what explicit assumption did CVM make about the distribution of microbial load?

A It -- the word explicit there -- actually, I'm not sure what you're fishing for. What explicit assumption did they make?

Q Please presume that I'm not fishing and just answer the question.

A Sorry. I don't know what assumption you're referring to.

MR. NICHOLAS: Your Honor, I object.

JUDGE DAVIDSON: What's the objection?

MR. NICHOLAS: If there is a place in the

document that counsel is referring to in the risk assessment, he should do that rather than ask the witness what the document says.

JUDGE DAVIDSON: Well, the witness has been told more than once that if he's unfamiliar with the material, he can ask for the document. I know you like to help him.

THE WITNESS: Your Honor, I do feel familiar with the document, but for explicit -- here's what they say about microbial load.

JUDGE DAVIDSON: Wait a minute. Let's not just pontificate every time you feel like it's important to do so. I think you're not answering the questions precisely. I'll allow you to explain every answer you give, but every time you get a question, it seems to me -- and I don't claim any scientific expertise whatsoever -- it seems to me that what you do is you anticipate what counsel is trying to show and you answer that instead of answering the question and then working on the anticipation of what he's trying to do.

For example, I heard him several times ask you

to listen for the words "microbial load." You didn't hear it, and yet every answer included reference to it. And I understand why, but the point is I want you to first answer the question and then if you feel you have to add some explanation, do so.

But the trouble is -- and you just said so yourself, you don't know what he's driving at so you can't answer the question. Well, you're not supposed to worry about what he's driving at at this point. If you feel that the answer you've given somehow leaves the wrong inference on the record, you can explain that.

THE WITNESS: Thank you, your Honor.

JUDGE DAVIDSON: Please pay careful attention to the question, try to answer it specifically, and then if you feel there's more needed, go right ahead and do so.

THE WITNESS: Thank you, your Honor. In this case your question is what explicit assumption did CVM make about microbial load. Is that correct?

BY MR. SPILLER:

Q Yes.

A Okay. I was hung up on which of the many assumptions, some explicit, some subsequently described, by CVM as being implicit but not explicitly stated you were thinking of. And I apologize for saying "fishing"; it's whatever you're thinking of.

The assumptions that they make -- I'm going to let "explicitly" go because, as I said, they talk about implicit later on and it's not clear to me what is now -- any more what's explicit and implicit. But what they say about microbial load, if that's your question, if I'm hitting the right target here, is --

JUDGE DAVIDSON: I'm sorry, Doctor. The answer is you don't know what he's referring to. You want to see what explicit -- you don't have to explain all the rest of it. You've already said you don't know --

THE WITNESS: I don't know what explicit assumptions you're referring to. Thank you.

BY MR. SPILLER:

Q I will try to look up a reference to offer you, Dr. Cox, and we'll come back to that.

A Thank you. Okay.

Q Turning to a different exhibit, which is already in the record, B-1886, the Rodriguez paper, and I think to put it in context, in your testimony on page 15 --

JUDGE DAVIDSON: I'm going to interrupt you, Mr. Spiller.

MR. SPILLER: Yes, your Honor.

JUDGE DAVIDSON: B-1886. It must have another number, because it's not listed here. It's not moved into evidence by Bayer.

MR. SPILLER: G-1711, I'm told, your Honor, is the corresponding number. I believe that's one of those that we discussed this morning that I failed to remember just now.

MR. NICHOLAS: I believe that's correct, your Honor, G-1711.

MR. SPILLER: Thank you, Mr. Nicholas. I apologize, your Honor, for the delay. I'm groping for the citation here.

JUDGE DAVIDSON: That's okay.

BY MR. SPILLER:

Q Dr. Cox, on page 15 of your testimony in the

top paragraph, the last sentence of that top paragraph, do you see a sentence that begins "second, it incorrectly identifies"?

A Uh-huh.

Q And the "it" there is a reference to CVM's risk assessment, specifically its hazard identification?

A Yes.

Q And your concern there, the defect that you see, is that FDA incorrectly identifies domestic chicken-borne Fluoroquinolone-resistant campylobacter as the predominant cause of adverse health effects, right?

A In this context, yes.

Q And you cite two papers by Cox and one by Rodriguez for -- and specifically Rodriguez you're citing for the fact that these effects are demonstrably caused by other factors, including foreign travel and restaurant dining. Am I right?

A Almost. The demonstrably is only partially covered. I'd say for Rodriguez it's suggested.

Q I hand you now what is printed -- marked with

B-1886 and which I have marked by hand G-1711 so that it will correspond correctly, and ask you if that's the Rodriguez paper.

A Yes. This is the Rodriguez paper.

Q And it doesn't have restaurant dining factored as a predominant cause, does it?

A I believe that it does. If you look at page 5 of the exhibit, the right-hand column, middle paragraph, beginning "only two factors were significantly associated with increased risk of campylobacteriosis, travel abroad and eating chicken at a restaurant or a canteen."

Q So it mentions chicken in a restaurant or a canteen, does it?

A Yes. That's right.

Q And in your quote you said it was restaurant dining, not including chicken, right? The not including chicken is my interpretation. In your quote, you didn't mention chicken like Rodriguez did.

MR. NICHOLAS: I'm going to object, your Honor. There's no quotation in Dr. Cox's testimony -- it's not quoting verbatim --

JUDGE DAVIDSON: Sustained.

MR. SPILLER: I acknowledge Mr. Nicholas' direction. The statement by Dr. Cox was not at that point purporting to be a quote.

BY MR. SPILLER:

Q Dr. Cox, I'll restate my question to avoid the error that I introduced, and I'm sorry for that.

A Thank you.

Q Do I understand that your allegation in your testimony is that contrary to FDA's viewpoint, it is not correct to attribute this to chicken, but you attribute it to restaurant dining and for that, you cite Rodriguez?

A That's a compound sentence. I cite Rodriguez to support the idea travel abroad and consumption of chicken in a restaurant are associated with being a cause, but that there is no statistically significant risk associated with consumption of chicken, other than in restaurants.

Q We'll agree, then, that the Rodriguez article includes chicken in its attribution of risk to restaurant dining. Is that correct?

A Well, again, what Rodriguez says, being careful to exactly quote his words, in the abstract on page 1, fourth line, sentence starting at the end of that line, where travel, he says two things -- two main things.

Travel abroad and consumption of chicken in a restaurant were statistically associated with being a cause -- so yes, he talks about chicken in a restaurant. But he continues -- "but" is my interpolation -- but "there was no statistically significant risk associated with consumption of chicken other than in restaurants."

Now, I cite this as suggestive, although not yet demonstrative, of the fact -- or of the hypothesis, I should say, that restaurants are the problem, chickens are not.

Q I wonder -- you say you cited it as suggestive and not --

A Conclusive. Right. Demonstrative.

Q -- demonstrative, but your testimony is that these are demonstrably caused by other factors. That's what your testimony says, right?

A It is. And as I said, I cited myself and my own causal analysis for the demonstrably part because Rosenquist didn't demonstrate, he only suggested.

Q And in this --

A Oh, I'm sorry. Did I say Rosenquist?

Q Yes, and I think you meant Rodriguez.

A I meant Rodriguez. Thank you.

Q And in the Rodriguez study that we've been looking at, they actually were able to explain only 20 percent of the Fluoroquinolone-resistant campylobacter cases. The chicken consumption in restaurants that you mentioned was the largest of those, and travel was the next of those, leaving approximately 80 percent unexplained. Am I right?

I'm sorry. I combined questions, didn't I? Am I right that chicken was -- chicken consumption in restaurants was the largest factor found by Rodriguez in that paper?

A I can -- do you want to give me -- are you looking at table 1?

Q Look at page 5.

A Yes. Uh-huh.

Q I think in the right-hand column, the paragraph that begins with only two factors --

JUDGE DAVIDSON: That's already been -- it's on the record. The witness, in answering a previous question, referred to that, so I don't think we need it a fourth or fifth time.

MR. SPILLER: Sorry, your Honor. Thank you, your Honor.

BY MR. SPILLER:

Q Now, moving to a reference also on page 15, you cite in the -- excuse me -- page 15 of your testimony, that's B-1901, the second paragraph, you show -- which I believe is G-1681 in this record --

A Uh-huh.

Q I'm handing you now a copy of that. I have one for the Court.

A Is it too late for me to add something to my response to your question about the Rodriguez paper?

Q No, that's why we have redirect, and there will be an opportunity, I'm sure, when your counsel asks you questions on that.

A Okay. Thank you.

Q You cite Michaud a number of times in your testimony, don't you, Dr. Cox?

A Michaud, yes.

Q You mention at page 20 of your testimony in the bottom large paragraph, about halfway down, at the beginning of the line you have Cox 2001 and then right after that, a recent prospective control study from Quebec, and that's where you cite Michaud --

A Yes.

Q -- identifies poultry as the principal suspected source of infection in only about 10 percent of the cases.

A Uh-huh.

Q You made that comparable to drinking tap water at home.

A He, I think, may have made it comparable.

Q And am I correct that that study did not determine any source in quoting 9 percent of the cases.

A Give me a moment, please.

(The witness examined the document.)

Q And of course read the entire eight-inch tall article, but if you look at the last line of the text

right above "preliminary results."

A Yes. Okay. So that sentence, the one we're looking at, says consumption of poultry, 10 percent and contaminated water, 9 percent, were the principal suspected sources of infection. The source was unknown, he says in 49 percent of the cases, although I suspect on the basis of what's here that it may not have been known in the other 51 percent as well, it says suspected versus known.

Q And am I correct, Dr. Cox, that in 48 percent of the cases the persons involved in this did not clean their cutting boards after handling raw meat or poultry and these were the cases and the controls answered that question, only 18 percent of them?

A You've asked me to answer a question that goes beyond what's shown here. The true percentage of the consumers who wash their hands after handling raw meat or presumably raw poultry is reported, but that's not the same as the true number.

So in other words, you have to -- it's as we were discussing yesterday. You have to bear in mind that these are responses to the surveys, so I can't

answer what was the true number. I can only say what the people that called --

JUDGE DAVIDSON: Doctor, I don't think you were asked to answer what the true number was. He referred you to a portion of the exhibit and he said -- I mean, I assume it's preliminary, otherwise why would he ask? It's already in the exhibit.

He asked you does it say that 48 percent of the cases -- cutting board -- and then you go and tell me that's not the true number. Well, that's not answering the question.

If it's a preliminary question, he just wants you to agree that that's what it says. Then he'll ask another question. If he doesn't, I'll rule the whole line out, okay?

THE WITNESS: But your Honor, it refers --

JUDGE DAVIDSON: But you're not testifying to what's in this exhibit. The exhibit speaks for itself. He's asking you --

THE WITNESS: Well, if he's saying doesn't it say this and it doesn't say that --

JUDGE DAVIDSON: It doesn't say 48 percent are

not cleaning --

THE WITNESS: It says 48 percent. It doesn't say 48 percent of cases.

JUDGE DAVIDSON: I see it says 48 percent of cases did not clean the cutting board after handling raw meat or poultry. Now, is that not what it says? I don't mean to interrupt or interfere, but the point is let's get to the question he wants to ask instead of belaboring what may or may not be the next question.

That's's what you're doing again. You're looking forward to what he's trying to show. Let's let him do it first.

THE WITNESS: Okay. Thank you. Yes, it does say that.

BY MR. SPILLER:

Q Dr. Cox -- in the next-to-last sentence, right?

A Yes. Your Honor is correct.

Q And isn't the signal in that that one of the differences indicated by the study is that people who don't clean the cutting board have a higher likelihood -- excuse me -- don't clean the cutting board after

handling raw meat or poultry have a higher likelihood of becoming a case instead of a control? And a case is a person who suffers from campylobacteriosis.

A Just a moment.

JUDGE DAVIDSON: Certainly.

THE WITNESS: Thank you. This article doesn't discuss or this abstract doesn't discuss whether the design is prospective, saying if you have poor kitchen hygiene are you more likely to get campylobacteriosis or whether it's retrospective, meaning if you got campylobacteriosis, it's more likely that you had poor kitchen hygiene.

Your question was is it more likely you're going to get sick if you don't wash your hands, if I understand it correctly. This may be showing if you ask people who are sick, hey, did you wash your hands, more of them will say no, which is the point -- the distinction I was aiming at before.

BY MR. SPILLER:

Q Did my question say anything about washing hands?

A Let me see. Washing hands -- so -- excuse me.

Cleaning the cutting board. I'm sorry.

Q So whether it's prospective or retrospective --

A Same issue.

Q It is the same issue, and isn't the signal here that persons who do not wash the cutting board after cutting meat or poultry were more likely to be cases than controls, whether mentioned on something in the past or prospectively?

A No. What it could be showing is that people who are asked, after they become cases, did you wash your cutting board, are more likely to respond no.

Q On page 56 of your testimony, Dr. Cox, you refer again to this paper. Let me know when you find that page.

A I'm there.

Q There are three paragraphs beginning with the word note, and in the second of those on line 3, you refer to the Michaud paper and you say that Michaud suggests at most a 10 percent fraction, right?

A Uh-huh. Yes.

Q Didn't we just agree that he only identified a

total of 19 percent?

A Of suspected --

Q I'm sorry. 51 --

A Go ahead.

Q He only identified a cause for roughly half of those, right?

A I don't believe he's identified any causes.

Q He only identified these sources, these factors.

A Yes. That's right.

Q And so do you agree it's not fair to say that at most 10 percent since any of the unattributed 49 percent could fall either in the eventually associated with poultry column or not?

A I don't think that's correct, but -- and the reason is what exactly does "unattributed" mean here. you know, is it unattributed because there was no evidence that this was the source? So let me take a minute to read this carefully again.

JUDGE DAVIDSON: I think we'll take a short recess. Be back at a quarter of.

(A brief recess was taken.)

JUDGE DAVIDSON: Mr. Spiller.

MR. SPILLER: Thank you, your Honor.

BY MR. SPILLER:

Q Dr. Cox, would you turn to page 25 of your written direct testimony, please?

A I will. Should I finish answering the question when -- you were waiting for my answer when we broke off.

JUDGE DAVIDSON: Okay. He's right. I don't remember the question, but I will have the reporter read it back.

THE WITNESS: Thank you.

(The reporter read back the record.)

JUDGE DAVIDSON: Okay. You can answer.

THE WITNESS: My answer is that I do not believe that that is unfair, and that I believe that it is suggested in the first sentence of his conclusion.

BY MR. SPILLER:

Q Dr. Cox, referring to Michaud Exhibit G-1681, if any of the cases where the cutting board was not washed after handling raw meat or poultry were attributable to not washing the cutting board after

handling poultry, wouldn't that raise the factor related to poultry to above 10 percent?

A Not necessarily, no. That's not how attribution calculations are done.

MR. SPILLER: I won't ask further questions about that exhibit, your Honor.

BY MR. SPILLER:

Q Now, Dr. Cox, would you turn to page 25 of your testimony?

A Uh-huh. Okay.

Q In the second full paragraph of that page, am I correct you firmly criticize FDA's model by saying that it lacked widely accepted intellectual foundations, offered meaningless numbers based upon concepts that are useless and it incorrectly interprets these meaningless numbers? You had all of those things in that paragraph, don't you?

A The paragraph is what it is.

JUDGE DAVIDSON: You're supposed to answer the question. We know the paragraph is what it is. We know it's on the record, but he's asking -- as I told you before, and I don't want to have to tell you again,

it may be preliminary to something else. If it's not, I'll rule it out myself. But it's a simple question, it's a simple answer.

Either it does or doesn't. You either agree or you don't agree, and you say it says what it says. I mean, that's not an answer. It's obvious. Everyone knows it says what it says. You were asked a specific question. Answer it or say you don't know or you can't answer it but you can't avoid it.

THE WITNESS: Thank you, your Honor. Those were fragmentary quotes.

JUDGE DAVIDSON: Well, then you don't agree that you said that.

THE WITNESS: Yeah.

JUDGE DAVIDSON: Okay.

BY MR. SPILLER:

Q Did you say within quote marks in that paragraph that FDA is based on a technically deficient concept such as, quote, average exposure for an average individual?

A Yes.

Q And you know, Dr. Cox, don't you, that FDA's

risk assessment did not rely on average exposures for average individuals?

A I do not know that.

Q Would you refer to the risk assessment, then, at page 69? The risk assessment is Exhibit G-953.

MR. NICHOLAS: I'm sorry, your Honor. What page is that?

MR. SPILLER: 69.

BY MR. SPILLER:

Q And on that page -- Dr. Cox, do you have that page?

A Yes, I do.

Q You find a paragraph numbered very near bottom 4(c)?

A Yes, I do.

Q And does it not there describe an annual value representing measurable human exposure to chickenless products and a number of sources?

A Yes.

Q Does that not describe a cumulative exposure rather than an exposure only calculated from averages?

A It looks to me like it says 50.8 pounds per

capita. Yes, I interpret it as an average.

Q And if I heard that right, which you interpreted as an average.

A I didn't say which I interpreted. Which I know, as I sit here, interpret as an average, yes, per capita. Uh-huh.

Q And was that the source of your attribution to the CVM risk assessment in your testimony at page 25, second paragraph, that CVM average exposure for an average individual?

A It was not.

Q I don't want to put you to read through this now but can you remember and help us find in this document any place where FDA said that it was the average exposure to an average individual?

A I believe that that phrase came not from this document but from part of the back and forth on the NOO page.

Q And so if -- it did, Dr. Cox, and we're talking about the risk assessment, which do you think is the most authoritative and prime source of what the risk assessment said?

A You mean the risk assessment itself or the CVM assessment?

Q Yes.

A I assume in the context of this hearing that what they have said about their use of risk assessment represents their use of what they meant about it.

Q And so knowing that disparity, for your testimony you chose to rely on an answer which may have had some attorney's mistake in it and characterized it to the risk assessment.

MR. NICHOLAS: I object, your Honor. There's no evidence of disparity --

JUDGE DAVIDSON: Overruled.

THE WITNESS: I don't believe that I relied -- no, I don't think that I did rely on this. Even your question about total versus average, since we're dealing with proportions, I have a hard time -- I don't think I relied on any such distinction.

BY MR. SPILLER:

Q So far as you can recall now -- and I apologize if this is a repeat question -- nothing that you can direct us to in the risk assessment where you

say it says the average exposure for an average individual --

A Well, let's get to it. If we look at -- I opened at random at a good place. If we look at page 19, there's a figure showing what kind of exposure is considered in quantifying human health impacts in this model.

Are we on the same page?

Q I'm on page 19. Are you on page 19?

A I am.

Q Got it. And we're looking for a mention in quotes of average exposure for an average individual.

A No. I'm not looking for those words. I am looking for these words: human health impact, lamda, is equal to some constant, k-res, times the pounds of chicken consumed with Fluoroquinolone-resistant campylobacter. And my point is that this is describing risks to a typical on average a representative consumer.

I know that's been stated and, you know, what's not here is what is the distribution of exposures for different people. So it's average

exposure.

Q I'll try a different way, Dr. Cox. In your testimony at page 25, that second paragraph, the quoted expression average exposure for an average individual, in quotes, I thought you were attributing that to the Government Exhibit G-953. I gather for right now we don't have a source for that.

What source did you indicate for that? Am I correct you indicated no source for that quote?

A That's correct.

MR. NICHOLAS: Your Honor, I'm going to object. There's no indication that this is a quotation from a source. I mean, it appears from the text that the witness is emphasizing a particular term or setting it apart, not that he's attributing the quote to the risk assessment or any other document.

JUDGE DAVIDSON: Now that you've said that, why did you quote it? Why is it in quotation marks?

THE WITNESS: Your Honor, I'm pretty sure that I was using their phrase. I said in some written comments that this risk assessment doesn't look at the exposures of individuals and CVM replied in substance,

at least in my memory, that they didn't need to look at the different exposures for different individuals, they were relying on the average exposure of the average individual.

I stuck that in quotes in my testimony because it seemed to be an important concept.

JUDGE DAVIDSON: Well, excuse me, but when you put quotes, doesn't that mean that you're putting something in verbatim?

THE WITNESS: It can mean that, and --

JUDGE DAVIDSON: Oh, I see. It can mean other things?

THE WITNESS: Yes. For example, you could say this is a, quote, hypothetical. It wouldn't have to be that somebody actually said that --

JUDGE DAVIDSON: That's one word. I understand that. But this is a statement, a fact.

THE WITNESS: Yes, it is, without attribution but as a distinguishing phrase. And as I say, I do believe that it is quoted from part of the record, but I can't put my finger on it right now.

JUDGE DAVIDSON: I hear your explanation.

THE WITNESS: Okay.

JUDGE DAVIDSON: I can't get away with that in my decision. I can't quote from something I remember someone said without being able to attribute it. I can't quote inaccurately or I'm going to be held up to ridicule.

THE WITNESS: As indeed I sometimes am.

JUDGE DAVIDSON: Okay. Thank you.

BY MR. SPILLER:

Q Dr. Cox, on page 18 of your testimony, in the last paragraph, do you say that CVM made the utterly ad hoc and demonstrably incorrect assumption that the probability of campylobacteriosis in a person is directly proportional to the quantity of chicken consumed?

A Sorry. I missed that. Page 18?

Q We're on page 18 of your testimony.

A Right.

Q The paragraph fragment on the bottom of the page.

A Oh, here it is. Yes. Absolutely. Yes.

Q And in the page that we were working on

before, the risk assessment, that's Exhibit G-953 at page 69, isn't FDA's concern not with only chicken consumption but with campylobacter-contaminated chicken consumption?

A Yes. And they are proportional to each other.

Q And in your allegation, did you mention that FDA's concern was with the quantity of campylobacter-contaminated chicken consumed?

A No. They're all proportional to each other.

Q On page 54 of your testimony, Dr. Cox, you have a parenthetical reference there, which I won't reread in the record, concerning AIDS and orange juice consumption.

A Uh-huh. Yes.

Q You're not really suggesting that there's a correlation or biological relationship between AIDS and orange juice consumption, are you?

A Certainly not a biological relationship. There may or may not be a correlation, and I mean to make no -- it's pure example.

Q And so would the point we should take from that be that you're reminding us that there needs to be

a biologically plausible hypothesis connecting the things if we want to relate something, for instance, like campylobacter in chicken to campylobacteriosis in humans?

A No. That's not the point that I intended. The point was that you can divide any aggregate quantity, such as number of campylobacteriosis Fluoroquinolone-resistant campylobacteriosis cases, by any other, such as pounds of chicken meat or estimated contaminated chicken meat consumed, and thus come up with a ratio. And that does not establish a relation between them, again, quoting from all the written discussion on this, in any meaningful or useful sense. This example was intended to demonstrate that point.

Q And in your written testimony from last December and in your testimony today, is it your testimony that the relationship between campylobacter on poultry and human campylobacteriosis is as remote as the connection in your remark about between AIDS and orange juice?

A I believe that the examples are -- I attempt to suggest that the aggregate -- I'm sorry -- the ratio

of aggregate level of campylobacteriosis cases to the aggregate level of chicken consumption has not been shown to have any stronger causal connection than other ratios, including manifestly ridiculous ones.

Q Thank you.

A Uh-huh.

Q On page 18.6 of your testimony --

A 18.6.

Q -- excuse me. On page 18. I refer to the .6 to help me remember that it's six-tenths of the way down the page.

A Got you. Uh-huh.

Q You say in the paragraph beginning dose response data, the second sentence -- and I just want you to confirm if I understand you correctly -- nonetheless, for its campylobacter risk assessment, CVM did not perform any dose response assessment. It has thus skipped the essential content of the risk characterization dose response step and failed to complete the steps required for a risk assessment as traditionally understood.

Did I get that right?

A Yes, you did.

Q When you reviewed this model in 1999, were you not aware of the design of FDA's risk assessment?

A When I reviewed this model in 1999, was I not -- when I reviewed the risk assessment I certainly read what was written about the design.

Q So you certainly knew in 1999 before you gave the evaluation in December of 1999 that we discussed yesterday that FDA did not have a separate dose response model within its risk assessment. You knew that at the time in December '99, didn't you?

A I have recommended -- I believe that I knew that, yes.

Q And you didn't say then that FDA had skipped an essential content and failed to complete a required step, did you?

A Can you please give me a copy of the document you're looking at?

Q You have a copy of the document I'm looking at, Dr. Cox. It's your testimony.

A In my recommendations in 1999, I believe I stated that the biggest assumption and the biggest

invalidated assumption and the biggest assumption that I recommended should be validated was the use of the big K in place of a dose response model. I believe I noted at the time that that assumption might be flawed and I recommended that it be validated before the model be used.

Q And you didn't recommend the dose response model then, did you?

A I did not recommend a specific parametric dose response model. In previous correspondence to David Vose that you mentioned yesterday, I had recommended putting in dose response information although not in those words. I used mathematical symbols.

Q If I gave you a copy of the transcript of your remarks there that we discussed yesterday, would you be able to find in it your explicit recommendation that the Center have a dose response model in its risk assessment?

A Not necessarily in those words, but certainly the concept, yes.

MR. NICHOLAS: Your Honor, Dr. Cox discussed the correspondence which I believe was G-1809 in the

testimony, which was G-1810.

JUDGE DAVIDSON: Okay.

BY MR. SPILLER:

Q Dr. Cox, I'm handing you what's marked with hand G-1810, copies provided yesterday.

A Thank you. This -- I'm sorry. Did you want me to find that pertinent passage?

Q Refer me to the part here where you explicitly recommend a dose response model.

A Beginning at the bottom of page 140, there are four lines in order. As you will -- I'm sorry -- and you will notice that the big assumption is that the incidence of bad outcomes more formally in response that we don't want is proportional to the volume of outgoing chicken informally the exposure, or something proportional to exposure.

I mean --

Q Dr. Cox, would you -- when you break from reading the transcript to us, would you let us know when you're breaking from that and to answer the question, would you find us the part that has an explicit reference in so many words to a dose-response

model.

A I told you I don't believe those words are there, just the concept.

Q Okay.

A And this is the place. And the next sentence, the one that says, I mean, big K is the key assumption in conjunction with the recommendations that at the end of this, that assumption be validated. That's what I'm referring to.

Q Dr. Cox, this is a very minor point but I'm really having trouble relating to your concept of quotation. I don't see the word "big" here. On 141, line 2, just now when you were reading to us in front of everybody, what you said -- did I hear you right? You said big K.

A Sorry. I thought you meant big assumption at the bottom. Yes, I said big K. Capital K. It's not a direct quote. It's a description of what's written.

Q Thank you. I now understand.

A Okay.

Q And I can simplify the question now based on your answer. Have you told me that this is the part

that you believe is the closest you came to an explicit recommendation that FDA include a dose-responsive model in its risk assessment?

A This is the beginning. As I say, you ultimately take it with the end which makes the recommendation and a more explicit recommendation was in my correspondence with David Vose saying if I translate the math, you've got to look at microbial load, you've got to look at those responses along with all these.

Q And it's possible we'll get to that but this was the meeting -- this, what I'm indicating Exhibit G -- what's the number on that?

JUDGE DAVIDSON: 1810.

MR. SPILLER: I'm sorry, your Honor.

JUDGE DAVIDSON: 1810.

BY MR. SPILLER:

Q 1810. In 1810, this was a public meeting, not just a correspondence with a single individual, David Vose, but this was a meeting at which the Center was asking and I think you testified had paid you for your evaluation of this.

A Uh-huh.

Q And you've told us the beginning of that and in a minute you're going to tell us the end. And have you confirmed -- I think you have but I want to make sure, that dose response model is not actually -- those words, dose response model are not actually here in G-1810.

A Right. It's exposure and undesirable or bad effect, not dose response. The words "dose response" are not there. The concepts are in different words.

Q In a risk assessment, Dr. Cox, isn't dose response in the -- I think you called it a traditional understanding of very explicit identifiable separate concept, a term used amongst experts for a specific thing?

A It covers a range of issues.

Q If you were speaking to a room that had other risk assessors, risk analysts in it as well as other scientists who were not risk analysts, what are the most descriptive terms you would use for a dose-response model?

A I'd have -- are we speaking about individual

level dose-response model, are we talking about a mixture distribution model for a population concerning --

Q I'm talking about the dose response model that you now say FDA should have included in its risk assessment that you were evaluating in December 1999.

A Oh, yeah.

Q If you're talking to a roomful of people and you wanted them to understand you were talking about a dose response model, wouldn't you have called it a dose response model?

A No. As I explicitly stated here, there are technical terms such as mixture distributions that I chose not to use. I spoke informally of munging together different parameters, said this was something that needed to be checked out.

Q Yesterday -- do I correctly recall that you thought transparency was an important characteristic in risk assessments, that they be explicit about their assumptions and that others be able to follow a risk assessment?

A I don't recall your saying that yesterday.

I'm trying to be responsive.

Q Thank you.

A First thing is to be correct.

Q If -- do you think it assisted in the transparency of CVM's risk assessment model for them to have posted on the Internet so that other people could see it and run it?

A Yeah. I don't like the word transparency but yes, I think making it open and inspectable and documenting the assumptions is all good things.

Q I'm showing you a copy of a book which I believe is partially copied in this record as G-1020 -- excuse me -- B, like Bravo, 1020.

I'm handing you B-1020.

JUDGE DAVIDSON: Your Honor, would you like a copy?

THE WITNESS: I hope the copyright laws have been observed.

BY MR. SPILLER:

Q Observing the law is very important, isn't it, Dr. Cox? You just mentioned that you hope the copyright laws have been observed.

Would it be of concern to you if people didn't observe the law in exchanging data concerning, say, drug approvals?

A I think you'd have to tell me more about the situation.

Q Well, the drug here is Fluoroquinolone, isn't it?

MR. NICHOLAS: I'm going to object, your Honor. This is beyond the scope of the witness' testimony. I don't see where it's relevant.

JUDGE DAVIDSON: He brought it up.

MR. NICHOLAS: I'm sorry?

JUDGE DAVIDSON: He brought it up himself. He just said he hopes the copyright laws are --

MR. NICHOLAS: Well, that's not related to the issue of a drug --

JUDGE DAVIDSON: Well, maybe it is, maybe it isn't. Let's see where it goes. If it's way out of line, I'll strike it all.

THE WITNESS: Okay. So do I believe there are some -- address the question again.

BY MR. SPILLER:

Q I'll ask a different question. Is it important in deciding issues concerning Fluoroquinolones, Enrofloxacin or Ciprofloxacin, that there be a truthful description of the circumstances of the drug as between all the parties?

MR. NICHOLAS: Your Honor, I'm going to object to the vagueness of the question. Trustful description of the circumstances --

JUDGE DAVIDSON: I'll sustain the objection.

BY MR. SPILLER:

Q Would it affect your testimony, Dr. Cox, if one of the parties to this hearing had agreed to plead guilty to a felony involving the intent to defraud or mislead the Food and Drug Administration concerning Ciprofloxacin?

MR. NICHOLAS: Your Honor, I'm going to object to that question as well. It's not relevant. There's nothing in the testimony with respect to that.

JUDGE DAVIDSON: Overruled. I want to hear the answer.

THE WITNESS: Nothing that I have testified to -- unless the fraud involved changing the raw data that

I analyzed, that unfortunate circumstance that was described would not be important to reaching the conclusions from the raw data that I reached.

BY MR. SPILLER:

Q What unfortunate circumstance do you mean?

MR. NICHOLAS: Your Honor, I'm going to object to this line of questioning.

JUDGE DAVIDSON: You have a continuing objection?

MR. NICHOLAS: It's absolutely irrelevant to this proceeding and it's prejudicial.

THE WITNESS: You said if somebody --

JUDGE DAVIDSON: Well, the jury will disregard it.

(Laughter.)

MR. NICHOLAS: I certainly hope so.

THE WITNESS: If somebody pleads guilty to a felony for something and it didn't affect the integrity of the data, would it affect my conclusions? The unfortunate circumstance was the scenario about the felony.

BY MR. SPILLER:

Questions do not constitute evidence. I don't care how much counsel pontificates. Answers are evidence. Some of it's good and some of it's irrelevant, but the answers are the only evidence, not the questions. So don't tell me I'm receiving evidence about this yet. I haven't.

The question was -- the witness has already answered it. He said he doesn't know anything about it.

Let's move on.

BY MR. SPILLER:

Q A hypothetical. If Bayer had agreed to plead guilty to that, would that affect your reception of Bayer's representations with regard to this drug in this matter?

MR. NICHOLAS: What drug is counsel referring to, your Honor?

THE WITNESS: What receptions? I started with the raw data that I got from CVM, not from Bayer.

MR. NICHOLAS: Dr. Cox, there's an objection pending.

THE WITNESS: I'm sorry.

JUDGE DAVIDSON: I'll overrule the objection, but I'm not happy with the tone of the questioning -- I shouldn't say tone -- the direction you're going in.

The witness has already stated on more than one occasion in response to this line of questioning that if you have something that says that the data that he reviewed was somehow tainted, then that might affect his -- otherwise, a corporation, of course not Bayer, could have committed holy murder, and it wouldn't affect his review of the data as long as the data was what he was looking at and not related to the fact that they somehow committed a heinous crime.

MR. SPILLER: I have and I will recite on this record -- I have no information that the data in the situation involved in my question was relayed through Dr. Cox. I will not ask further questions of Dr. Cox on this.

JUDGE DAVIDSON: Thank you.

BY MR. SPILLER:

Q In the partial copy of your book before you, Dr. Cox, that's Exhibit B-1020, on page 24 of the exhibit -- what page of the book does that correspond

to, Dr. Cox?

A It looks to me like page 113 here.

Q Thank you.

A Surely.

Q Does it indicate that your simulation model -- excuse me. And you describe at numerous places in this book your work with respect to campylobacter that AHI commissioned, right?

A On some of it, yes.

Q And on that page in the first full paragraph, third line --

MR. NICHOLAS: Excuse me, your Honor. Are we on 113 of the book or page 24 of the --

JUDGE DAVIDSON: They're the same, I believe. 24 of the exhibit and 113 in the book.

THE WITNESS: Uh-huh. Okay. I'm with you.

MR. SPILLER: I want to be fair to counsel to make sure that we have given counsel a full deck. Apparently, like me, counsel got a much abbreviated copy and I meant to give them the same copy that I had given to Dr. Cox.

Let me offer counsel a copy of Dr. Cox's book

which we bought so he can see page 113.

BY MR. SPILLER:

Q In the first full paragraph there, Dr. Cox, is there a reference to where your model is said to be available on the web?

A Back in 2001, yes.

Q And from your reference back in 2001, we agree it's not available now?

A I was not aware of that but I'll take your word for it.

Q Would you know when it was taken down or when it became unavailable?

A I would like it to be available and I would have to talk to our webmaster to find out.

Q When you used your model, did you ever discuss in any of your publications concerning that model what happens if in your model your change the prevalence of contaminated carcasses while leaving the bacterial load distributions constant?

A First, I don't remember the answer to that question. There's -- I've done numerous sensitivity analyses in different publications and showed a great

many curves, and that may have been one of them.

But secondly, I'd like to let you know that I have had more than one model. When you say your model, this is an early version.

Q In your testimony, you mention your model in several places. Is the final version of your model the one reflected in Exhibit A-17, the final report for AHI dated February 20, 2001?

A No, it is not. Not by a mile.

Q In your testimony, Dr. Cox, in all of the references to your model, where did you tell us which was the final version of your model?

A It depends if you're referring to Cox 2002, then it was the 2002 model. If you're referring to Cox 2001, it was the earlier model. I've worked on a model over a period of years and different publications would peg a different version of the model.

Q In your testimony, did you say at some point this is the final model and give a cite to it where --

A I don't believe so.

Q You agree in FDA's risk assessment FDA did keep the bacterial load distribution constant?

A If I may answer a little informally, for everything that mattered they did, but there are some sensitivity analyses involving log exponential distribution in which I believe they varied microbial load distribution.

Q Thank you for both parts of that answer. In your model -- and this time when I'm referring to your model, I'm referring to Exhibit A-17. And I don't believe I've given you a copy today, have I?

A I don't think you have.

Q I'm handing you now Exhibit A-17, a dynamic simulation model of campylobacter illness, final report, prepared for the Animal Health Institute.

MR. SPILLER: Excuse me, your Honor. I gave you a copy yesterday. I believe I asked you if you would save it for today.

MR. NICHOLAS: I don't believe I got a copy yesterday.

MR. SPILLER: I'm looking now to see if we have an extra copy.

MR. NICHOLAS: I have together all the documents I believe we received.

MR. SPILLER: Handing counsel for Bayer a copy of Exhibit A-17.

MR. NICHOLAS: Thank you.

BY MR. SPILLER:

Q On page 29 of that, Dr. Cox --

A Hold on. I'm looking for it.

Q I apologize. I've given you a bad page number. In the exhibit, do you have page 111?

A I do.

Q And does that correspond to page 29 at the bottom?

A Yes, it does.

Q Am I correct that your model assumes that any dosage below -- and we're talking here a dosage of campylobacter -- below 500 CFU has a zero probability of producing an illness?

A Not really.

Q I'm sorry. I'll quote. In your model, does the phrase occur, and I quote, our model assumes that any dosage below 500 CFU has a zero probability of producing an illness, close quote?

A Yes. The report said so at that time. As I

say, but not really.

Q And in -- I'm sorry. Did you say that's not really the case? That's what the report says but that's not really the case?

A Yes. Subsequent sensitivity analysis showed that assumption was unnecessary.

Q But you still represent that it's true.

A Let me say yes to make things easy. As I say, there are multiple runs of the model, there are multiple versions, and there are extensive sensitivity analyses. In some of those sensitivity analyses, that simplification was relaxed. It didn't make any substantial difference, but it was relaxed. So at this time, those sensitivity analyses hadn't been run.

Q However many times you ran it, did you cite for that 500 CFU minimal infected dose, Robinson 1981?

A Yes, I did.

MR. SPILLER: I'm sorry, your Honor. I'm lost in my paper. I'm looking for a copy of that paper.

JUDGE DAVIDSON: All right. Off the record.

(Off the record.)

JUDGE DAVIDSON: Back on the record.

MR. SPILLER: Thank you, your Honor. I apologize for my delay.

BY MR. SPILLER:

Q Do you know, Dr. Cox, how many test subjects were involved in the research that led you to use that figure?

A I see that as being a compound question. First, I don't remember how many test subjects were used in Robinson. Secondly, I don't agree that I used that figure and I would cite in the exhibit that you handed me, B-1629, my statement that sensitivity analysis provides partial solution to the problem of unknown variable dose response relations.

MR. NICHOLAS: Excuse me, your Honor. We seem to have G-1816. I'm not sure we have the same exhibit as the witness is referring to.

JUDGE DAVIDSON: All right. We'll straighten it out.

MR. NICHOLAS: Is this the --

MR. SPILLER: You have an advance copy of an exhibit that the witness doesn't have now.

MR. NICHOLAS: Okay.

MR. SPILLER: The pending question is whether or not he recognizes -- excuse me -- whether or not he knows how many study subjects were in the Robinson study on which he relied.

THE WITNESS: And I'm telling you --

MR. NICHOLAS: Excuse me, I'm still --

THE WITNESS: I'm sorry.

MR. NICHOLAS: The Robinson study is what exhibit? I was just handed G-1816.

MR. SPILLER: And it was a great mistake of mine to hand it to you because I was only giving you an advance copy of something that I was about to hand the witness.

MR. NICHOLAS: But as I understood, you handed the witness Robinson?

MR. SPILLER: I have not handed the witness the Robinson paper.

MR. NICHOLAS: Okay. Sorry.

JUDGE DAVIDSON: All right. Come on. Let's move on.

MR. SPILLER: Okay.

THE WITNESS: Did he say anything to me?

JUDGE DAVIDSON: I don't think so, but I'm not sure. Do you have a question pending, Mr. Spiller?

MR. SPILLER: The question pending included, as he pointed out, two parts, one, that you don't have any subjects. I believe he's indicated that he doesn't.

BY MR. SPILLER:

Q And the second part, that I thought was routine, that you relied upon -- and am I correct, Dr. Cox, you're explaining to us why you didn't rely on it?

A I'm reading my previous written description on that subject, yes.

Q The description that we're inquiring about is the description in Exhibit A-17.

A Yes.

Q And the paragraph that begins on page 111 of that exhibit, that begins the minimum infective dose. And you say in the second sentence, other research has shown that the minimum dosage may be as low as 500 CFU (Robinson, 1981). I thought that meant you were citing Robinson for that. No?

A Of course it means I was citing Robinson.

What I was not relying on as I have clearly written is any assumption that there can't be any risk below 500 CFUs. And as I've written in Exhibit B-1629 on page 36, any dose response relation with these qualitative features that are discussed tends to produce similar expected number of CB cases from given population frequency distribution microbial loads.

I'm not relying, in any way, on that 500 number.

Q But you said it in the model that you did for AHI --

A That's what I'm explaining. That's an early model.

Q And you've identified that model in your testimony here as a model you were relying on.

A Oh?

Q Excuse me. That's a question. Did you?

A No. Not to my knowledge.

MR. SPILLER: Now, your Honor, I'll hand the witness what has been marked, and counsel has a copy of, G-1816.

BY MR. SPILLER:

Q Dr. Cox, looking at that one-page exhibit in the lower left-hand corner, does it identify the author of that article as D.A. Robinson?

A Yes, it does.

Q And is that article about 8 inches tall in one column?

A Let's say it is. Yes.

Q A short article. How many study subjects got the dose of -- got any dose in that study?

A This is one guy administering to himself.

JUDGE DAVIDSON: Say that again? I didn't --

THE WITNESS: He gave himself the dose. This is one subject.

JUDGE DAVIDSON: Okay.

BY MR. SPILLER:

Q So in this study, one subject got one dose one time. Am I right?

A Yes.

Q And that dose was 500 CFUs.

A Uh-huh.

Q And he got sick. He got abdominal cramps and mild diarrhea, didn't he?

A Yes.

Q And this is the paper that in A-17 you relied on to establish the minimal dosage as low as 500 CFUs.

A Yes. This is the paper that I relied on for that 500 CFU number. Yes.

Q Now, a moment ago, were you reading to me from G-629?

A I'm sorry. Can you tell me --

Q A moment ago, I was taking you back. You picked up another exhibit and you said something else. Was that 629?

A No, I think it's 1629. I'm reading from my book.

Q Okay. Let me give you Exhibit G-629.

A 629. Okay.

MR. SPILLER: I believe this is in evidence, your Honor.

BY MR. SPILLER:

Q You relied on this in you're a-17?

A A-17 being --

Q I'm sorry. The AHI report. It's labeled final report.

A I cited it.

Q Okay. Thank you. That's satisfactory for the present purpose. Are you aware that this Tunis article that you cited, the beta-Poisson dose response model that you use for the probability of infection, assumes that one can get infected from just one bacterium?

A I realize that from the model, yes.

Q And are you aware that that dose response model that you used for the probability of illness given infection assumes that one can become ill from just one bacterium, not just that you get infected but that you can get ill?

A Yes, I'm familiar with that assumption.

Q Isn't your arbitrary threshold in A-17 of 500 CFU therefore inconsistent with using the Tunis model?

A It is not. As I -- should I elaborate?

Q Only if you need to to be responsive to the question. I understand you to have said you don't believe it's inconsistent. Is that right?

A That's correct. And for the reasons previously cited.

Q Have you ever seen the combined Tunis dose

response model described in G-629 at page 7, figure 2(c) -- I should let you find that.

A G-629.

Q G-629, page 7, figure 2(c).

A Yes.

Q Have you ever seen that combined model being used in any other microbial risk assessment?

A Have I seen -- I'm hung up on the word "used." I've seen it cited in other mi -- may have to say microbial risk assessments or antimicrobial risk assessments.

Q Yes. I'll refine the question. In other study in this record, is there any indication that you know of that the Tunis model has been used to prepare a risk assessment for a microbial or antimicrobial?

A Well, hold on, please. This is going to take me a minute.

JUDGE DAVIDSON: Off the record.

(Off the record.)

THE WITNESS: I am not aware of this -- hold on a second. The Rosenquist, et al. paper does not cite this paper of Tunis, et al. Now, I can't quickly

tell whether it cites the same combined model to which you refer. So it's definitely beta-Poisson model. Whether it's the identical model would take me a little more work.

In addition, I don't remember -- and I think you asked whether anywhere in the record has this been used, if I'm remembering your question correctly. I believe that the record somewhere discusses the WHO groups -- oh, yes.

In Curtis Travis' -- that's where it comes out. It talks about the use of the WHO, made in its model and its valuation. But that's all I can do while I sit here.

BY MR. SPILLER:

Q So we can find that in, it's your recollection, the testimony of Curtis Travis in this record.

A Yes. He cites the WHO discussion and says that the beta-Poisson model is a good model and is adequate.

Q And is it your testimony that whatever that is that we'll find in Dr. Travis' testimony applies to the

combined Tunis model as depicted on page 7 of G-29 in figure 2(c) like Charlie?

A No. It's my testimony that I don't remember whether it was the combined model.

MR. SPILLER: Your Honor, I am about to lapse into statistics, which will take me a while.

Would it be appropriate to begin lunch recess now so that I could be more efficient?

JUDGE DAVIDSON: Any objection?

MR. NICHOLAS: Do we have any indication how long we're going to --

JUDGE DAVIDSON: We haven't gotten into that.

MR. SPILLER: In connection with my commitment yesterday to let us finish today, your Honor, I'm very hopeful of finishing by 2:00 to enable any direct to be completed during the day.

JUDGE DAVIDSON: You mean you think you have about an hour, hour and 15 minutes more altogether?

MR. SPILLER: Yes, your Honor.

JUDGE DAVIDSON: Okay. We'll adjourn until 10 minutes to 1:00.

(Whereupon, a luncheon recess was taken.)

AFTERNOON SESSION

(12:45 p.m.)

JUDGE DAVIDSON: On the record.

Counsel for Bayer and the witness are not back yet, so we'll wait for them. The record will reflect it is a quarter to 1:00.

Off the record.

(A brief recess was taken.)

JUDGE DAVIDSON: On the record.

It has come to my attention that I may have gone on the record five minutes early, but all I said was we'll wait, so there's nothing for you to worry about.

MR. NICHOLAS: I apologize, your Honor.

JUDGE DAVIDSON: No, you weren't late. I think it's me. I was five minutes early.

MR. NICHOLAS: Thank you, your Honor.

JUDGE DAVIDSON: Mr. Spiller? Let the record reflect that the witness is still under oath and Dr. Cox is still available for your brief cross-examination on statistics.

MR. SPILLER: Thank you, your Honor.

BY MR. SPILLER:

Q Dr. Cox, you have your final report, Exhibit A-17, in front of you?

A Yes, I do.

Q Would you look at page 111 and 112, please? I'm sorry. Look at page 112 first.

A Okay.

Q And your figure 2.5 is your dose response probability curves by age group. Taking, if I may, just focus on the bottom one, that would be a plot using the Tunis combined model as we described before, right?

A I believe that's correct.

Q And the Tunis paper you also have in front of you, Exhibit G-29, page 7. You have that before you? I'm referring to the page number on the little exhibit stamp in the upper right-hand corner.

A And which page number do you refer to?

Q Page 7.

A Yes, I do.

Q And just for illustrative purposes and not to introduce, I have a blowup here. You should refer to

the official exhibit. I'm going to be tracking along here because those figures are small for my eyes.

Am I right that his combined model is depicted in figure 2(c)?

A Yes.

Q And if I understand the description of that figure correctly, it looks like there are three curves, a solid -- I'll call it a smooth hill with sloping edges as the middle curve and quite a jagged dotted line above it, and a much smaller dotted line below it.

Do those dotted lines represent the fifth and ninety-fifth percentile confidence intervals above that plotted line?

A I don't know offhand. I can read the --

Q All right. I should let you have a chance to do that. Read the legend at the bottom of figure 2 of Tunis page 7.

A Yes. These are confidence intervals for bootstrap replicates. Yes.

Q And I don't know the statistical term. To me, that looks like a whopper of an upper confidence limit. Dr. Cox, is it the case that at approximately 10 to the

second -- that would be 100, right?

A Uh-huh.

Q At 100 CFU, the confidence intervals for that value on this plot would range roughly from zero to 60 percent probability of illness, right?

A The bootstrap replicate confidence intervals, yes.

Q And it's good, careful science to define the confidence intervals about data. Is that right? Or about plots.

A Depending on how you do it, confidence intervals often don't indicate model uncertainty so they may not be useful in the context where the model was uncertain.

Q Is it a good thing in both models and statistics to be explicit about depicting and describing uncertainty?

A Yes. Extremely important.

Q And he did that here.

A Well, he was explicit about the resampling the bootstrap replicate variability. He's not really characterizing model uncertainty. As you can see,

outside the range of the data there's a lot of uncertainty.

Q Now, one thing that jumps out even to a non-mathematician is Tunis's mountain seems to have two sides to it but I notice your dose response curve on page A-17 produced using that combined model only depicts one side of the mountain and it gets up to the top of the mountain and then it's cut off, but actually using that model, the values plotted would decline as the doses got higher, wouldn't they?

A If you extrapolate outside the range of data.

Q And as a matter of fact, isn't it the fact, Dr. Cox, that using that model, the combined Tunis model that you chose, if the dose went all the way up to 10 to the eighth, that would be a hundred million colony forming units, that the Tunis model would predict a near zero illness response?

A It may. You know, I could find myself with a range of data.

Q Well, let me show you for -- excuse me. One other thing about the dose response curve that is depicted in your final report, Exhibit A-17, figure

2.5. That doesn't show your 500-CFU cutoff, does it?

A Not in that plot.

Q And if we were to draw that, it would be, wouldn't it, a vertical line somewhere between log 2.5 and 3, wouldn't it?

A Yeah. Yes.

Q This is for illustrative purposes only and is not evidence. I have a depiction here of smooth-sided hill with slopes on either side, roughly corresponding, doesn't it, the dark line, assuming that -- the line from the margin at the lower left all the way over to the far right, corresponding to log 10 -- excuse me -- log 8. That roughly corresponds to the shape of the Tunis combined model plot, doesn't it?

A Over that -- over the range that you're showing --

Q And that's the range that he showed, isn't it? If you look at the exhibit you have, G-629, the Tunis paper, page 7, figure 2(c), he covers the range from -- well, he goes from -- yes, ten to the zero to ten to the eighth, right? And that's the log ten to the zero, log ten to the eighth, that's what's depicted in this

example.

A Okay.

Q And so the 500 CFU cutoff would be a vertical line, I'm indicating with red just for illustration purposes, at about log 2.7, here. So the actual -- when I say here, I'm indicating a vertical line extending from the Tunis plot down to the X axis of about log 2.7.

So your model, because it includes the 500 CFU cutoff, actually includes a cliff on the side of the hill, doesn't it?

A Well, no. My model states -- or my description and discussion of exactly this issue in my model states that risks are low or zero. They don't have to be zero, they can be low for sufficiently small doses, e.g., less than 500 CFUs, doesn't have to be 500 CFUs, and illness probability increases rapidly as a function of dose reaching an approximate plateau -- this is now describing why I deal with this model in my model -- it reaches an approximate plateau of about .2 for CFU levels of about a thousand to 10,000 CFUs.

What I've said is by doing sensitivity

analyses, I've found that any dose response model that captures the rough qualitative features of the data will suffice. So I'm not -- I forget the exact word that you used but I'm not assuming a cliff and I'm not assuming anything that's strange behavior outside the range of the data in terms of declining risk.

Q On page 111 of Exhibit A-17, Dr. Cox, right about the paragraph response rate by age, there's a smaller paragraph and in that smaller paragraph a sentence that begins our model.

A Uh-huh.

Q That's your model and your partner, Douglas Popkin, right? Your associate?

A Yes. That is our February 20, 2001 version of the model, before the sensitivity analyses in the final form were published.

Q And that model -- excuse me -- that statement says our model assumes that any dosage below 500 CFU has a zero probability of producing an illness, doesn't it?

A Yes.

Q And a zero probability of producing an illness

on the Tunis plot, figure 2(c), would be along the X axis, wouldn't it?

A Yes, it would.

Q And it would continue flat with zero probability on the X axis from the origin to the point that corresponds to 500 CFU and then it would ascend vertically to join the rest of the curve, right?

A Yes, that's correct.

Q So that would indicate that for all doses between zero and 498, the zero probability of illness, zero at 498, zero at 499 and at 500 CFU suddenly the response would be 20 percent of the population, right?

A Yes. That would be the approximation.

Q In this record, do you know of any observed database where either humans or chickens were observed to have responded in that way to a series of doses such that there was no response at 498, 499 and 20 percent response at 500?

MR. NICHOLAS: Your Honor, if I may, I object. Chickens don't respond. The question is compound and improper.

MR. SPILLER: I volunteer to rephrase my

question, your Honor.

JUDGE DAVIDSON: Go right ahead.

BY MR. SPILLER:

Q Dr. Cox, in this record, is there any data set that indicates that humans respond in such a way that the dose response would be plotted as no probability of illness up to 498 or 499 CFUs and a 20 percent response in humans to campylobacter at a dose of 500 CFU?

A Can you remove the front exhibit to show the poster with number 1257 on it? Thank you.

If you look at those data, you'll see that assuming that there's zero response to zero dose, the pattern as far as we know is that not much happens and I don't believe that there are data for humans below about 500 CFUs. Well, not in this experiment.

Basically, not much happens until you get up to a few hundred CFUs, then about 20 percent of people get sick. So I think that these data from one feeding study -- it's hard to know what to make of them but they're consistent with the idea that there's a higher response probability when you have several hundred, several thousand CFUs. And we don't really know what

happens in the low dose range.

JUDGE DAVIDSON: Let the record reflect the witness is referring to Exhibit G-629 page 7, the figure thereon, when he said 1257, which happens to be the page number in the actual publication as opposed to our exhibit number.

THE WITNESS: Thank you, your Honor.

BY MR. SPILLER:

Q Dr. Cox, my question was whether or not you could indicate in this record a human dose response at data plot. Did you indicate that you believe that Tunis at the reference just cited is such a plot that shows a sudden change at 499 where there's no response to 500 where there's a 20 percent response?

A No, he didn't look at 499 so no, I don't think he shows what happened below 500.

Q So we agree that he did not show but I haven't gotten an answer to my question about whether there is anything in this record that indicates there is any human dose response curve to campylobacter plotted that would show a sharp break in the dose response curve such that there is no response at 498, and none at 499,

but a 20 percent response at 500?

A I'm not aware of any data that contains 498 and 499 and I believe that these data -- well, I think these data support the usefulness of the approximation that I made.

Q And your assumption about the -- your assumption in A-17 at page 111 that any dosage below 500 CFU has a zero probability is based on Robinson. What is the statistical significance of such a determination based on a single dose single human study?

A Well, first I disagree with the premise embedded in your question. I've tried to be really clear that I did not assume that 500 CFUs is a magic threshold.

Q I stand corrected. You did not assume. Your exhibit says that our model assumes, and I thought we had established previously that our included Dr. Cox.

A Of course it includes me. It does not in any way depend upon the assumption. At the time of this early exhibit I had not yet done the sensitivity analyses that I've reported and published subsequently.

Q And in A-17, where do you describe the uncertainty about this value?

A In A-17, I had not yet done the sensitivity uncertainty analysis so they are not yet described. That came subsequently.

Q They're not described in A-17. Is that right?

A Right. They're in B-1029.

Q In your final model report to AHI, Exhibit A-17 at page 110, near the top of the page, a subparagraph numbered 3, you have an assumption one chicken provides four servings, the CFU count per simulated chicken is divided by the number of servings. The dose response model is then applied to each serving.

Did I read that right?

A Yes, you did.

Q Then for a serving to have at least 500 colony forming units in your model the carcass from which it was derived would have to have had 2,000 CFUs, right?

A Let me first correct something that you said in asking your question and then answer your question. You referred to this report as a final model report. I

want to again state that this was the final report of an initial modeling project that has subsequently led to additional runs, additional sensitivity analyses, additional data, and there has subsequently been peer review to published. So I wouldn't want this to go on the record as being the final model report. It's the final report of a preliminary model.

Within that context, yes. To get 500 CFUs on one serving, you would need 2,000 CFUs on one chicken.

Q And 2,000 CFUs or 2,000 of anything is about 3.3 log to base 10, is that right?

A That sounds right.

Q So referring in A-17 to your figure 1.5, and that's on page 104, 3.3 logs would be very near the tiny skinny toe at the right-hand side of that curve. Is that correct?

A Yes, it would be in the right-hand tail of this distribution.

Q So if this distribution of microbial load on a carcass is even slightly wrong, it would probably have an enormous effect on your model's accuracy, wouldn't it?

A No.

Q Well, let's say --

A Not on the accuracy of the conclusions which, as demonstrated in the subsequent sensitivity and uncertainty analyses are extremely robust, the assumptions.

Q If that plot in that exhibit, we compare the value at log 3.3 and if it were shifted only to log 4 so it would go from 2,000 to 10,000, there would be a change from a very small amount to none, is that correct, in this plot?

A I think you're misinterpreting the plot.

Q I'll withdraw the question then. I don't want to misinterpret.

In your testimony at page 23, in the first paragraph -- let me know when you have that.

A Okay. I'm there.

Q You testified that CVM, by assuming its model form is correct, despite overwhelming evidence to the contrary --

A Yes.

Q Is this overwhelming evidence to the contrary

that the risk increases disproportionately with microbial loads above 500 CFU, simply the dose response model that we've been talking about?

A No, it is not. It's the observation that most people eat a lot of chicken and most people don't get sick.

Q On page 10 of your testimony, Dr. Cox, you mention the traditional risk assessment steps and you note there in the sixth numbered paragraph that uncertainty characterization is one of the steps. Am I correct that you agree that that's important?

A Yes, I do.

Q And in your final report to AHI, dynamic simulation model of campylobacter illnesses, Exhibit A-17, page 14 -- excuse me -- page 96, for the first parameter, you did provide a characterization of uncertainty. Am I right?

A A partial characterization, yes.

Q And for all the others you did not, right?

A That's incorrect. For example, if you look at the colonization index, a bilinear probability equal to .90, that number specifies an entire probability

distribution.

For the next one down, another bilinear distribution, the one number specifies entire distribution. For the surface microbial load which starts to get exciting from a cause and effect point of view, as specified, a triangular distribution for the lot of 10 of the values.

For the one beneath that, transportation factor -- and so forth.

Q In the triangular distribution that you mentioned as significant, is that a description of variability or a description of uncertainty?

A Yes.

Q You've answered assuming that I was asking if it was one or the other. Are you indicating that it is both?

A For a full explanation of the interpretation of these distributions, I would refer to Exhibit B-1029 starting on page 36.

MR. NICHOLAS: Excuse me. I believe the reference is 1020, not 1029.

THE WITNESS: Thank.

JUDGE DAVIDSON: Thank you.

THE WITNESS: Thank you.

BY MR. SPILLER:

Q Is that description, Dr. Cox, a description of variability?

A There's a false dichotomy here. These distributions are used in the simulation model to approximate both uncertainty about model parameters and variability in the microbial load that will reach individuals.

And there's a substantial framework that these piece by piece steps get into to justify that dual role and that is the framework outlined in the exhibit that I just referred to, the B-1020 -- in my book.

Q And in your risk model for campylobacter described in the book, and I think you have an excerpt of the book there that you've been referring us to, B-1260, and in the A-17 report, you used data, didn't you, from studies by Stern, et al. to arrive at your estimate of initial microbial loads? Matter of fact, that's the source of the triangular distribution that you just cited me to, isn't it?

A It's a source of the data.

MR. NICHOLAS: Your Honor, I'd just like to clarify which exhibit we're talking about. I know Dr. Cox's book is B-1020, so it doesn't --

JUDGE DAVIDSON: It's B-1020. You said B-1260, Mr. Spiller.

MR. SPILLER: I did say that. I acknowledge the correction. I believe both of those refer to it but counsel is correct that the version in front of the witness is 1020. I'll settle for A-17 at the page we were discussing, page 96.

BY MR. SPILLER:

Q And, Dr. Cox, you referred me to the surface microbial load, triangular distribution, Stern, et al. That's one of the papers you relied on, right?

A I again want to stipulate that reliance is too strong a term because of the sensitivity and uncertainty analyses but Stern is the data source for this distribution of the model, yes.

Q And it's the only source that you cited for that particular --

A In this role of the table, yes.

Q I'm handing you now Exhibit B-712, which I believe is in the record.

A Thank you.

Q Dr. Cox, is B-712 the Stern paper to which you refer?

JUDGE DAVIDSON: Excuse me again. In the record as what -- with what number?

MR. SPILLER: The only number I have is B-712, your Honor.

JUDGE DAVIDSON: Well, based on my records here, B-712 has not been moved into evidence.

MR. SPILLER: I move Bayer's Exhibit B-712 --

JUDGE DAVIDSON: Wait a minute. It may be that it has another number.

MR. SPILLER: It may be, and I apologize, your Honor. I don't have a conversion table with me. I think for purposes of discussion, even if it were not an exhibit, we can cover the point.

JUDGE DAVIDSON: All right. If it's not in otherwise, we'll deal with it subsequently but right now you can refer to it as B-712.

MR. SPILLER: Thank you, your Honor.

BY MR. SPILLER:

Q If you look in B-712, Dr. Cox, at page 3, table 2, and page 4, table 3, are those the sources of the data that you used for the parameter described that we just discussed in A-17, page 96?

A Sorry. Oh, for the surface microbial load?

Q Yes.

A Okay. Which two tables again, please?

Q Table 2 on page 3 and table 3 on page 4.

A Yes.

Q And you know how those levels were determined.

A Not in detail.

Q It's described in the paper.

A Uh-huh.

Q On page 2, the right-hand column under sampling and microbiological analysis --

A Yes.

Q I'm sorry. When I said paper I'm referring to B-712. I'll let you read it quietly. Let me offer a description and you see if I've got it fairly.

You put the bird carcass in a bag and you massage the dead bird carcass so that some of the

bacteria are rinsed off the carcass. You put the rinse aid in a centrifuge, you spin it down, you plate the resulting materials, you grow it out and you count the colonies.

Is that a crudely fair description?

A That pretty much matches my understanding, yes.

Q So to know how many bacteria were really on the bird, you couldn't call the result of that plating the surface microbial content unless you knew what your percent recovery was from that rinsing, right?

A When you say the bird, which bird are you referring to?

Q The birds that are subjected to this process to determine -- to get the values recorded. I assume that there are a number of birds.

A I assume so, too, and I think there's a distribution of measured values as a result of this process for those birds. Bearing that in mind, could you re-ask your question, please?

Q Don't the values recorded from such a carcass rinse procedure necessarily and persistently understate

the actual bacteria counts on the bird because the rinsing process cannot recover 100 percent of the bacteria on the bird?

A This is a matter of what the operational definition of the numbers mean. My operational, I mean what measurement procedures are we using.

I agree with you that if you mean -- if you count the CFUs on the bird using a different procedure, would you get a different or possibly greater answer, I would agree with you.

Q You fitted triangular probability distributions to these data, did you not, Dr. Cox?

A Fit is a little bit strong but we approximated a mean and variance by triangular distributions in this case.

Q So for instance, in Exhibit A-17 on page 99 under the paragraph with the heading initial level of exterior infection microbial load, in the second sentence --

A I'm sorry. I'm not finding it.

Q We're in Exhibit A-17, page 99, near the middle of the page, you see a paragraph headed initial

level of exterior infection?

A Oh. The heading. Yes. Yes, I do.

Q And then in that paragraph, I think the third sentence is a triangular distribution for the log to the base 10 of the value captures these three points. You have a T in parentheses zero, 298 and 638. Is that correct?

A With one --

Q I'm sorry; 2.98.

A That's right. That is correct.

Q And you state just above that the distribution there ranges from zero to ten to the 6.38 in the preceding sentence.

A Correct.

Q Where in Stern's paper does it say -- I'm sorry. The first of your triangular values there, in the parentheses you have a zero. Is that a minimum in the triangular distribution?

A Yes. That's the minimum of the three parameters shown.

Q Where in the Stern paper does it say that a minimum of zero CFUs were observed?

A I'm not sure that it does.

Q So if you only cited Stern for this distribution and he didn't say zero, how can you put a zero in?

A Well, the way a triangular distribution works, as discussed more fully in the uncertainty and sensitivity analyses as I've referred to several times, is that one has a plausible lower bound, a plausible upper bound and a plausible central estimate.

The distribution is not intended to be completely physically accurate. The distribution is intended to capture the approximate mean and variability for use in something called the central limit theorem that comes in later. That's the substantial framework that I referred you to earlier. And in this case, zero would be a plausible lower bound.

Q And 6.38 logs is the highest level Stern observed, correct?

A That sounds right. Uh-huh.

Q And by using that triangular distribution with that maximum value you exclude the possibility of any

higher value like 7 or 8 load?

A I do not. That point is specifically addressed in the uncertainty and sensitivity analysis that I've referred you to many times. The --

Q I'm sorry. Is that the analysis that's not in A-17, it's somewhere else, it's in your book?

A It's the analysis in my book and in other publications, yes.

Q Thank you.

A The point there is that mean variance for each step in a process where a number of factors are being multiplied is sufficient when there are a large number of steps, as there are here, fully characterize the distribution, the meaning of the variance for the overall process.

Q Thank you.

A Uh-huh.

Q The center number in that triangular distribution, the 2.98, is that a calculated value?

A I believe that it is. It's been a few years since I've done this but I believe that reads like a geometric medium and -- data points.

Q And for a triangular distribution, it's supposed to be the geometric median, not the average?

A As I've explained, a plausible upper bound, plausible lower bound and something that's about right as a measure of central -- whether it's the median, .6 mode, makes no difference because at the end I'm going to use the central limit there.

Q In you're a-17, did you provide any visual demonstration of the degree of fit of these triangular distributions?

A You mean --

Q The goodness of fit.

A Goodness of fit of the triangular distributions to?

Q The data.

A No, not for each individual step. And again you understand that to be irrelevant in the context of this.

Q You mentioned a moment ago the central limit theorem.

A I did.

Q Did I understand you, that's the distribution

of -- does that include the fact that a distribution of the mean of a random sample from a population has a standard deviation that is proportional to one over the square root of the sample size?

A No, that's got nothing to do with it.

Q That has nothing to do with the central limit theorem?

A No.

JUDGE DAVIDSON: Need some time?

MR. SPILLER: Yes, your Honor.

JUDGE DAVIDSON: Okay. Off the record.

(Off the record.)

JUDGE DAVIDSON: Back on the record.

MR. SPILLER: Thank you, your Honor.

JUDGE DAVIDSON: Okay. Let's go.

BY MR. SPILLER:

Q Dr. Cox, I'm passing you what's been marked G-1817. Dr. Cox, G-1817, does that appear to be a partial copy of Fundamentals of Biostatistics by Bernard or edited by Bernard Rosner?

A It looks that way, yes.

Q And would you refer within that to the book's

page 158?

A I'm looking at it.

Q At the top is there a boxed definition or a description of the central limit theorem?

A Yes, I would say a central limit theorem. Yes, there is.

Q Do you agree with that definition?

A It leaves out some technically necessary conditions, so it's an approximate statement to the central limit theorem. For example, this would be incorrect if the population had a certain distribution, but it's an approximation to it, yes.

Q The -- using the central limit theorem, isn't it true that a mean of a random sample of 25 measurements would have one-fifth the standard deviation of the population's distributions?

A I'm sorry. Would you repeat the question?

Q Isn't it correct, then, that if one took a mean of a random sample of 25 measurements, the mean would have one-fifth of the standard deviation of the population's distribution?

A You mean the sample mean?

Q Yes.

A Well, actually, for 25, a rough rule of thumb is -- you chose a bad example. You would use the T distribution for 25. But I take your point. It's a square root relationship.

Q The data you used from Stern's paper, and we're now looking at B-712, are geometric means of samples sized 10 and 25, right, referring to those same two tables, table 2 and table 3?

A Yeah.

Q And those are geometric means, right?

A Uh-huh.

Q So for the sample size 10, the square root is about 3 and the samples of size 25, the square root is 5. So fitting the triangular distributions to these mean data and using those fitted distributions as if they represent individual carcasses, you would actually have underestimated the standard deviation of the carcass load by a factor of somewhere between 3 and 5, wouldn't you?

A No. No. Not at all. That's not how it works. I mean, you're talking --

Q If -- I'm sorry. Finish your answer.

A Keep on going. But no, we're not talking about sample standard deviation and sample mean of the components of the overall process. The sample limit theorem that I referred to deals with the composition of multiple multiplicative steps. We're not even approximately in the same ballpark here.

Q Dr. Cox, in your testimony at page 7 --

JUDGE DAVIDSON: Getting tired, Mr. Spiller?

MR. SPILLER: Yes, your Honor, and I'm hoping to finish soon.

BY MR. SPILLER:

Q On that page, Dr. Cox, at line 15 of your paragraph 7, you note your opinion that banning Baytril will greatly increase human health risks and you expect the ban to cause more than 25 additional days for each hypothetical day of Fluoroquinolone-resistant campylobacter illness prevented.

A Yes. That's my opinion.

Q That conclusion arises from your risk assessment model, doesn't it?

A In part, yes.

Q So if the model is unreliable, the conclusion is also?

A No. It's only partially derived but there's a much simpler argument to getting there that's much more data driven.

Q In your testimony at page 37, there's a chart there, linear --

A Yes.

Q You plot the total chicken concerned -- I think you call that totchick on the X axis.

A Total chick, yes.

Q Against the case rate on the Y axis.

A Yes, that's correct, although the interpretation -- it's not exact because I don't have measurement for these seven FoodNet areas of the actual chicken consumed. I had to construct a proxy from survey data that I had.

Q Nonetheless you fit a layer of direction through them to show that the slope was negative, right?

A I fit a simple linear regression to see what the slope would be.

Q And that's one of your bases for calling CVM's assumption that cases are proportional to chickens consumed incorrect, the fact that you got --

A No. This particular diagram is what's called an ecological study. No, I didn't rely on this one. It shows --

Q You didn't rely on this but you include it in your testimony?

A Yes, that's correct. It shows the point without going through nearly as much detail as the full broad data analysis.

Q And even though you don't rely on it and you say in the first bullet on that page plotting CP case rates against the summary of self-reported and per capita chicken consumption for FoodNet catchment area reveals a negative association -- that's your italics -- negative association between them, consistent with the results from the CDC and case control studies? Am I not correct in saying that that you did rely on that plot?

A Yes, you are incorrect. No, I didn't rely on it because you might be able to remove one or two

points and change the answer in something that only has 7 data points. What I relied on was the underlying data, which is a lot richer but this is the simplest way of showing the results.

Q You picked the regression equation for this?

A The statistics package that I was using in the upper not clearly legible margin of the picture.

Q And according to your testimony, that's the relationship.

A Was that the end of the question?

Q Yes.

A I'm sorry. If that's what relationship?

Q That's what you intended to indicate CVM's incorrectness by depicting that negative association?

A Again, the really convincing evidence here is from the individual data analysis. This is aggregated analysis by, I think, seven FoodNet sites. So I don't consider this by itself to be -- this isn't the overwhelming evidence that I'm speaking about. This is like shadow analysis.

Q And did you show your statistical analysis for this plotted line -- for instance, did you show the

confidence interval?

A No. This is just exploratory.

Q Did you show the R square values?

A No.

Q It's only exploratory but you have it in your testimony for us.

A Sure. What I'm saying is if you take the simplest possible look at the data, you'll see it doesn't look anything like straight line sloping upward to the right. That's my point. That's what CVM assumes; it's not even proximately true.

Q And if you plotted 7 completely random points in a two-dimensional space like a chart, isn't there a 42 percent probability that you'd get a higher R square value than your analysis revealed for these points?

A That sounds plausible to me.

Q Doesn't that demonstrate the fragility of the point you've made here and therefore that we'd need to show some measure of confidence about the data you portray?

A No. I keep saying this is an exploratory analysis that is designed to show the simplest possible

way of looking at the data. I already showed that what I referred to as the K model doesn't come close to fitting the data. I see no reason to calculate R squareds or to calculate confidence intervals to make this point. I do see a need to do those things when we do the serious data analysis.

Q So if it's serious you would explain that this is exploratory but for your testimony you didn't identify this as exploratory.

A I don't think I used the jargon exploratory data analysis. I think I have indicated in multiple places that the simplest way of looking at the data that the hypothesis, that it's a cluster around a straight line leaning from the lower left corner upwards has no relation to the real data even when you look at it in the simplest possible way.

Q You called this I think just now in your testimony today an ecological --

A This is an ecological presentation, not because it has anything to do with the ecology but because the data is collected at the FoodNet area level.

Q So in your analysis, as depicted in your testimony, did you include the ecological confounders?

A I did mention -- I believe I mentioned that there were several risk factors that were significant at this ecological level and several suggested confounders. So I think I did mention that probably -- yes, I think I mentioned it but I couldn't swear to it.

Q Are they mentioned close enough to this part of your testimony so that you could point me to it on this or the nearby page?

A Well, this testimony was written with hyperlink in it and they were very close based on hyperlink but I'm not sure how close they are in terms of pages.

Q The cite in your book to your model was a hyperlink also, wasn't it, Dr. Cox?

A That was a URL.

Q Are both of those ways of referring from a computer document to a web site, for instance.

A No. The hyperlink within this document are to locations within the document.

Q Are you suggesting that the printed version of

your testimony that the Court and that the Center have enable us to jump from one point of your document to another?

A No. I'm not. I'm just saying that the way I wrote this and intended for it to be used, there are hyperlinks all over it to get from point to point. But we can't do that in the version --

Q Intended for who to be able to use it that way?

A First and foremost, me.

Q And the rest of the world who didn't have your document in electronic format didn't have that ability.

A CVM had my document in an electronic format.

Q The version filed in this record --

A To my sorrow, PDF translation lost the links so what we have is less convenient than what I wrote. Same words.

Now, I'm sorry. What was it --

Q Whether there was something on the adjacent pages of the version that is before you now of your testimony includes a description of ecological confounders for this ecological depiction?

A Oh. I don't remember where confounders -- I'm sorry. I don't know.

Q Each of the seven points that you've plotted there represents a different FoodNet catchment area, right?

A I would be very -- no, I don't think these points would represent FoodNet data -- represent FoodNet areas at all.

Q I'm sorry. I was misreading, I suppose, in your testimony at page 37, right above the chart. I thought it said linear aggression case rate against total chicken consumption in seven FoodNet catchment areas. What did I miss there?

A I thought you had used the word "represent" to imply that FoodNet data represents the states from which they're taken or represent the larger population.

Q So do we now agree that each of the points plotted on your testimony, page 37 in that plot, you meant to refer to 7 different FoodNet catchment areas?

A That's correct. Or actually the samples that are taken from those areas.

Q Surely those different areas reflect areas

with different eating habits, environmental factors, different localized poultry sources. There would be substantial differences from the areas from which that data derived.

A I think there are huge differences in all of those respects, yes.

Q And where on this or adjacent pages have you explained to the readers or your testimony that factor?

A Which factor?

Q The factor that these data points are derived from different areas with different unidentified ecological confounders?

A Give me a minute, please. Oh, well, here. First, I don't believe that I give any additional discussion of this figure beyond what we've covered. I may have referred to it elsewhere.

Right in this bullet point it says plotting CP case rates against a summary of per capita chicken consumption for FoodNet catchment areas. The plot is self-explanatory in terms of there being wide differences in the case rates. You can see they go up almost as high as 34 and they go down about as low as

5.

I don't think I have a written discussion of what the data show beyond what's already discussed.

Q And did you extend this analysis, Dr. Cox, in your 2002 publication to do multiple linear regressions on just 7 points?

A Yes. Yes, I did.

Q Again, in that circumstance, without uncertainty analysis, right?

A Well, you know, I would say that --

MR. NICHOLAS: Your Honor, could I know what document counsel is referring to, please?

MR. SPILLER: I'm referring to, as I indicated in the question, his 2002 model. I believe that's Exhibit B-1252.

MR. NICHOLAS: Is that in evidence, B-1252?

MR. SPILLER: It's a Bayer exhibit. I don't know.

MR. KRAUSS: Yes, it is.

MR. SPILLER: I apologize, Dr. Cox. The lawyers have interrupted your answer.

BY MR. SPILLER:

Q I think the pending question was in that one -- and I can hand it to you if you want, but am I correct, there is no uncertainty analysis on this one either in this plot?

A I'm a little slow to go along with either. I think uncertainty in this ecological analysis is fairly well expressed in the scatter plot. You can see that the points do not fall on a straight line. There is some scatter in the scatter plot.

Moreover, I note right underneath it that while these data suggest that aggregate chicken consumption is not positively associated with the risk of CP illness unless one forces -- use CVM's model, for example, several other factors do appear to be significantly associated.

That immediately antecedes the article that you're now referring to where which specific factors that vary from site to site are significantly associated are listed.

Q So the analyses, both in your testimony and in B-1252, you would agree is reflective of the quality of

your analyses of the CDC data set.

A Oh, by no means. This is an exploratory analysis.

It's just a picture saying hey, let's take a look at the data. And that's -- what I was taught when I took statistics is you should always start by looking at the data.

But that's hardly where you end. That's just the beginning.

MR. SPILLER: I think the beginning is a good place for me to end, your Honor.

I have no further questions on cross-examination of Dr. Cox.

JUDGE DAVIDSON: Okay. We'll take a short break while you change positions. I assume you have some redirect?

MR. NICHOLAS: Yes, your Honor.

JUDGE DAVIDSON: Okay. And when we come back on, the first thing we'll take care of is the rest of these exhibits, because I think I've got them in a little bit of a mess here.

We're off the record.

(A brief recess was taken.)

JUDGE DAVIDSON: Back on the record.

REDIRECT EXAMINATION

BY MR. NICHOLAS:

Q Good afternoon, Dr. Cox.

A Good afternoon.

Q I'd just like to clear up the record. Would you tell us how your Ph.D. degree reads, what it says on it, the degree?

A It says Louis Anthony Cox, Jr. is awarded the Doctor of Philosophy in risk analysis. And I believe it also gives the name of the department, Department of Electrical Engineering and Computers.

Q Is there any doubt in your mind or does anybody else have that question, whether you have a doctoral degree in risk analysis?

A None. I have a doctoral degree in risk analysis.

Q There was testimony yesterday with respect to a meeting. I believe it was described as the Boston meeting, and you were presented with what I believe was an abstract from that meeting that -- and this is

Exhibit -- I think it's G-1811. It's a little hard to read. Entitled "International Journal of Infective Diseases."

MR. SPILLER: You're right, Mr. Nicholas. G-1811.

BY MR. NICHOLAS:

Q Dr. Cox, would you open that and tell me if it describes the participants of that meeting? Mr. Spiller, if I recall correctly, asked you whether there were any people who were basically government people, or he seemed to imply non-affiliated people with this case.

A I don't see a list of participants.

MR. NICHOLAS: Your Honor, if I could mark for exhibit the actual journal this came from, which would be, I believe, 1948, I believe, your Honor.

JUDGE DAVIDSON: Okay.

MR. NICHOLAS: And I'm going to show this to counsel if I may because I don't have an additional copy, your Honor.

JUDGE DAVIDSON: Well, then, you better not mark it. I mean, show it to counsel -- if it has to be

put in the record, we'll put it in but right now you can't put it in. You don't have enough copies.

MR. NICHOLAS: Your Honor, this is the only one I have.

JUDGE DAVIDSON: What am I looking at?

MR. NICHOLAS: The page on the left, your Honor.

JUDGE DAVIDSON: All right.

MR. NICHOLAS: Thank you, your Honor.

BY MR. NICHOLAS:

Q Dr. Cox, I am going to give you this, which I'd like to mark 1948 --

JUDGE DAVIDSON: You can't mark it.

MR. NICHOLAS: I'm sorry.

BY MR. NICHOLAS:

Q Dr. Cox, let me give you this journal article -- journal, rather --

JUDGE DAVIDSON: Excuse me. I don't mean to interrupt you but what's the purpose of this, so he can read the names of the people that are there?

MR. NICHOLAS: No, I'd just like to refresh his recollection, your Honor.

JUDGE DAVIDSON: I understand, but for what purposes?

MR. NICHOLAS: For that purpose --

JUDGE DAVIDSON: Well, then he can read those names into the record. Mr. Spiller has looked at it, he can look at it again to make sure it's accurate. We don't need the document, particularly because you don't have copies for everybody, and you leave me at a disadvantage if I'm going to move it in or mark it.

MR. NICHOLAS: I'm sorry, your Honor.

THE WITNESS: I see I blew my reply yesterday.

BY MR. NICHOLAS:

Q And, Dr. Cox, does this refresh your recollection as to who were participants at the meeting?

A It does. And I had forgotten -- I think I said no government people showed up, and I was wrong about that. Of course Dr. Fedorka-Cray was there, and --

Q Was someone from the American Veterinary Medical Association there?

A Uh-huh.

Q And to your knowledge was that person a witness in this case?

A No.

Q And to your knowledge is that person employed or otherwise affiliated with Bayer?

A No.

MR. SPILLER: I apologize for interrupting, Mr. Nicholas. Since I don't have that in front of me, could we name the person being described at the AVMA?

THE WITNESS: Lyle Vogle. And then Paula Fedorka-Cray, from the FDA.

BY MR. NICHOLAS:

Q And are there other people, to your knowledge, who were at that meeting whose names appear on the participant list who are also not witnesses in this matter, if you know? Just tell us who they are.

A There's my friend and colleague Kim Thompson from Harvard University. You just want folks who are not witnesses?

Q That's correct.

A Well, let me embarrass myself here. There are a fair number of names here I don't recognize as being

witnesses.

Q Would you pick up exhibit -- tell me what number is on there, please?

A It's Exhibit G-1811.

Q And you have there -- is the list of participants included in that exhibit?

A I still do not see a list of participants here, no.

Q Thank you, Dr. Cox. Now, Dr. Cox, Mr. Spiller asked you about whether you provided advice to Dr. Vose and whether you were paid as a consultant for that and whether you provided advice to the FDA with respect to risk assessment and whether you were paid with respect to that, and then I believe he went on to question you specifically about whether in your 1999 appearance before the -- at the workshop on risk assessment hosted by CVM and whether in your correspondence with Dr. Vose, whether in those instances you had specifically used the word dose response. And I'm referring now to G-1810 and G-1809.

MR. SPILLER: Object to the form of the question. I don't believe I asked about the

correspondence with Vose. I know that I did ask about the transcript reflecting the December '99 meeting.

JUDGE DAVIDSON: That's my recollection. That's all right. When he asked the question, you brought up and said it referred to the question and he said -- answering you out of position because he's not supposed to talk to you, Mr. Spiller said your counsel will take care of that on redirect.

But he only talked about 1810.

MR. NICHOLAS: I'm sorry, your Honor. I stand corrected. Dr. Cox did in fact, I believe, respond to G-1809, the correspondence, as well, and I'd like to give the witness copies of G-1809 and G-1810, unless he has copies there.

THE WITNESS: I have a copy of G-1810, but not G-1809.

BY MR. NICHOLAS:

Q Now, Dr. Cox, would you review those, and is it true that you did not use the term "dose response" in either of those documents?

A Based on a quick review, I think I did not use the words, although I did use the concept.

Q And could you explain why you did not use the words?

JUDGE DAVIDSON: I think he's already done that.

THE WITNESS: Well --

JUDGE DAVIDSON: Excuse me. He was asked the same question by Mr. Spiller and he said I didn't use the words, but what I said was the same as using the words. He went into great detail about which portion of which word and he said -- I forget the exact word he said, but in even reading the quote, he said something to the effect "that means."

If you're going to add something to that, that's fine. If you're going to have him repeat it, I don't want to hear it.

MR. NICHOLAS: No, your Honor, my intent was not to have him repeat that.

JUDGE DAVIDSON: Okay.

MR. NICHOLAS: Thank you, your Honor.

BY MR. NICHOLAS:

Q Dr. Cox, would you please explain why you did not use those words?

A I will. I initially thought that the assumption that I now like to call the big K assumption, which is the human health risk, is directly proportional to pounds of contaminated chicken consumed. That originally sounded plausible to me, and my colleague, David Vose, suggested that's how he was looking at it based on his understanding of physics and the situation or the physical situation.

And I later became very full of talk about the dose response relation, because as I recommended to CVM in a 1999 document, the G-1810, I went to try to validate the assumption that the big K framework is essentially correct -- not correct in every detail, but the basic, risk, increases in proportion to exposure.

And I quickly found out, as soon as I got some real data, that that big assumption -- what I called the big assumption or the key assumption, excuse me -- it just doesn't fit the data.

So then I thought, well, why not? I mean, intuitively, what is it that we're missing? Then I started to talk to CVM and anyone who would listen about microbial load, dose response, the fact that

people who have exceptionally high exposures, the people with exceptionally high microbial loads in their food, those are the ones who are getting sick.

And that's when I started to say things like the average has got nothing to do with it. We've got to look at dose response. And at that time, I began to use dose response very explicitly, because this comes down to a dose response and microbial load exposure issue and I didn't understand that back in 1999, so I only raised it in a theoretical possibility and went on record to say that I expected that when CVM validated it, it would find that it was no big deal.

I was very much mistaken in that.

Q I believe I'm correct that when Mr. Spiller was questioning you he made -- a fair number of times he emphasized your final risk assessment, your final report, document A-17. And then he went to some length to ask you questions about it and whether it accurately portrayed various aspects of the risk assessment, whether some exceptions were explicit or implicit and whether you had various qualifications.

Can you tell us what this document represents,

whether it was your final -- I believe you testified it wasn't your final risk assessment, but could you explain what this document is and whether it evolved or not?

MR. SPILLER: Object to the question. It's already been asked and answered.

JUDGE DAVIDSON: The witness has already explained it was not his final. He said what it was. I mean, the last time I gave you an opportunity to put something on the record that you hadn't put on before, you went way beyond the scope of the questioning on cross and I don't want that to happen again.

MR. NICHOLAS: Yes, your Honor.

JUDGE DAVIDSON: In other words, he's already explained it's not his final, that it was -- he explained what it was.

MR. NICHOLAS: Your Honor, if I may, I'm asking him to explain the evolution of this because the way it was presented is even though it's not his final, he was questioned about the details of this and this is an early document and I think it's important for him to be able to explain how this document evolved into

something that --

JUDGE DAVIDSON: I'm sorry. I sustain the objection. It's been asked and answered.

BY MR. NICHOLAS:

Q Dr. Cox, did you confirm the models other than this model?

A Yes, I did. As I tested different assumptions, and sought to validate modeling functions that seemed reasonable to me initially, I found that several didn't fit the data and needed to be changed.

So, for example, it's not just the big K framework, but I eventually noticed that the attributable number of cases formula was the wrong formula. It actually doesn't calculate anything that's useful for predictable attributable number of cases. So that led to a revision in my model formulas.

I noticed that ruling and appendix inappropriately overwrote the data with prior opinion, that a certain fraction could be .5 even though the data set was .06 and that that was done over and over again. And so I published a series of corrections and versions of the model as I came to understand better

the limitations in the initial model.

Q Have your further models been published?

A They have. Not all of them -- one of them went through a review process at the Society of Risk Analysis and was presented with a Best Paper Award last December. The process now moves into a journal review, and that takes a while. It has not yet been published.

Q And during the course of your various revisions, did you have discussions with CVM, with CDC, with other parties, or was this something you did totally private?

A I had initially some discussions with CVM. We had a lot of casual conversations about we should get together for a day and really take a look at the data and try to work things out and come to a shared understanding.

And once David and I got together for at least part of the day, I think, under the joint auspices of AHI and CVM. But then CVM pretty much stopped responding, and then I started drafting comments and sending those in and never got any response to those.

So for a while, yes, but no.

Q Have you attempted to validate your model?

A I have.

Q And can you tell us what efforts you took to validate your model and the results, please?

MR. SPILLER: Object. Not within the scope of the cross.

JUDGE DAVIDSON: You're going beyond the cross examination. Sustained.

BY MR. NICHOLAS:

Q Let me turn now to page 30 of your testimony. I believe yesterday with respect to bullet 2 on page 30 of B-1901, Mr. Spiller questioned you fairly extensively on some of the references there, Effler, Kassenborg and so forth and so on.

And I believe he was trying to draw a distinction between what the papers said and what your conclusions were. Did you rely on anything else in reaching your conclusions with respect to this paragraph, this bullet point?

A The major conclusion in this paragraph is restaurant dining that we spent so long on yesterday. Yes. As stated here -- actually all it states is it's

consistent with. What I relied on was the raw data. What I primarily relied on for my understanding is analysis of the raw data of Effler and the individual -- I'll just call it raw data -- the individual level data from the CDC case control study, which I think is the best source, that also underlies Kassenborg here.

Then I did go to the literature including these sources and I looked to see -- well, look, if it's a restaurant problem and not a chicken problem, what are other people finding. And as I -- perhaps we adequately covered yesterday, there are papers such as that of Rodriguez which, if read in their entirety, fairly show that other people are thinking along the lines of the same things.

But I relied on the raw data and on my analysis of that data as the primary basis for my conclusion.

Q Just so there's no confusion, when you say you relied on the raw data, could you please explain what you mean?

A Well, that means I like to use an analytic approach. Suppose we don't know anything about what

causes what? Suppose we don't know anything about model form, whether it's exposure is proportional to risk or something else? Is there some way to let the data itself speak?

And there is such a way. There is a body of methods known as non-parametric methods. I applied these standard techniques in packages such as SAS that anybody else can run, they're very verifiable, they're very objective. And I used them to test certain hypotheses.

Ones that are most interesting to me are what causal hypotheses are consistent with the data? For example, is the causal hypothesis that there are excess days of diarrhea from Fluoroquinolone resistance? Is that something that we can test with the data? And for some data sets, for example, the CDC data set which is a great data set, the answer is yes.

So in general, I rely on the raw data and then I rely on canned statistical packages or commercial packages that run analyses. And in the ideal world, I just dump in the data, push the button and say what does it show.

JUDGE DAVIDSON: And you got that from the question of what data you relied on? That's the answer to that?

THE WITNESS: No --

JUDGE DAVIDSON: Well, that's my problem with you, Doctor. You -- the question was would you describe what data you relied on, and you went on to a lot of other things which may or may not be interesting.

When you said that you relied on the data, what did you mean?

THE WITNESS: I thought that was the question, yes, and I assumed that question mean --

JUDGE DAVIDSON: Well, I would like to hear what data you relied on as opposed to, you know, how you went about it and all the other ramifications, because I've got you -- you've referenced publications.

THE WITNESS: Now --

JUDGE DAVIDSON: Now, the publications I see, some of it has a lot of data in it, some of it has very little data in it. It makes it difficult for me to see what you're talking about.

THE WITNESS: Your Honor, I apologize for being not clear. To me, none of the publications we've talked about has any data.

JUDGE DAVIDSON: Okay. So then you went behind that?

THE WITNESS: Yes.

JUDGE DAVIDSON: In each one of those publications and you looked at the raw data. How did you get it?

THE WITNESS: Only three. I looked at the raw data for the CDC publications, which are actually more than three, the Friedman publication, Kassenborg --

JUDGE DAVIDSON: I'm talking about the Rodriguez, the --

THE WITNESS: There I got the Effler raw data. I originally sent an e-mail and asked for it, and he wouldn't give it to me, and then it was gotten for me I think under Freedom of Information.

So I got the Effler data. I got the Smith data. And those three data sets are the primary basis that I --

JUDGE DAVIDSON: That's what I wanted to hear.

Okay.

THE WITNESS: Okay.

JUDGE DAVIDSON: Proceed.

MR. NICHOLAS: Thank you.

BY MR. NICHOLAS:

Q Now, there was a fair amount of questioning this afternoon about a dose response model. Do you believe that your risk assessment accurately portrays the incorporation of appropriate dose response modeling and have you validated that? And by risk assessment, we can start with your 2001 draft report, A-17, and to your latest risk assessment of the publication that I believe you referenced as B-1262.

MR. SPILLER: Objection. Beyond the scope of cross.

JUDGE DAVIDSON: You're asking him for an awful lot of material just on the basis of the fact I believe you were questioned about dose response. If you're going to ask him questions to explain his answers on cross, I'd be glad to let you do that but you're giving him a platform for another 20-minute lecture and I don't want that.

MR. NICHOLAS: Your Honor, that wasn't the intent --

JUDGE DAVIDSON: I know that, but that would be the result when you ask a question that has that many things in it.

MR. NICHOLAS: Well, Mr. Spiller spent the better part of an hour, I believe, asking Dr. Cox about dose response.

JUDGE DAVIDSON: I understand.

MR. NICHOLAS: And I'm trying to narrow this down, your Honor.

JUDGE DAVIDSON: Well, narrow it, otherwise it's going to go all over the place.

BY MR. NICHOLAS:

Q Dr. Cox, on page 29 -- I'm sorry -- on page 37 of B-1901, which is your testimony, Mr. Spiller asked you a number of questions about the -- what I would call a graph that appears on that page under the title linear regression, et cetera, et cetera. Do you see that?

A Yes.

Q Is there anything -- do you believe that this

is still an accurate presentation with respect to the issues discussed on this subject -- under this title?

A I do.

JUDGE DAVIDSON: That's enough. You already said that before on cross.

BY MR. NICHOLAS:

Q How does your final model deal with dose response?

MR. SPILLER: Objection, your Honor. I believe that's beyond the scope. I don't think we ever got into the final model, although we dealt with the models that we had in the testimony.

JUDGE DAVIDSON: My recollection is the witness referred to it himself but it wasn't part of any of your questions, so I'll sustain the objection.

BY MR. NICHOLAS:

Q Dr. Cox, could you explain how the model in your textbook, B-1020, deals with dose response?

A Yes. The issue of dose response modeling and of uncertainty about the dose response relation was dealt with explicitly there by saying we don't know what the true dose response relation is. Can we try a

bunch of different dose response models that are all passing through the data, so the only thing they have in common is they're consistent with the data; does that change the results?

And that technique, called sensitivity analysis, is what allowed me to reach robust conclusions despite uncertainty about the details of dose response model. And there's a fuller discussion, of course, in that reference.

Q Now, with respect to Exhibit A-17, which is a -- referred to by Mr. Spiller as your final report about two years ago, do you rely on that document for your testimony?

A No. No, I don't. My testimony is mainly about the CVM model.

Q And to the extent you're discussing your own model in your testimony, do you rely on that -- on the discussion in A-17?

A No. As I've stated, that was an early model before I understood that the attributable risk form was wrong and that other things were wrong. So I do not rely on that.

Q How critical -- I'm sorry. Strike that. And I believe you testified that you had attempted to validate the CVM model?

A Yes, I tried to fit key assumptions to the data, yes.

Q And can you tell us briefly how you tried to do that and what the results were?

A Yes. I obtained three what I refer to as raw data sets, the three I referred to a few minutes ago, so the CDC case controlled data, the Smith data and the Effler data. And first thing I noticed is that those sources raised the apparent anomaly of chicken consumption at home being associated with reduction in risk and chicken consumption in restaurants no.

So that made me think well, big K -- there probably needs to be more than one K in there and the algebraic form that risk is proportional to exposure can't be right for all the different groups that were exposed. It certainly can't be right for groups who were exposed at home.

So then I set out to say, okay, that big simplifying assumption isn't right, what can we do

instead. And I used a non-parametric method based on what's called causal graph analysis to figure out how different factors relate to each other and how to back out confounding effects.

Finally, I adjusted for non-causal relations between exposure and risk. What I mean by that is just the point that males, for example, turn out to be -- whether or not they eat chicken, they're at greater risk of campylobacteriosis than females, so that you might want to have a different K for males and females.

What I did was to form an analysis that said is this a direct causal -- is the data consistent with this being a direct causal relation or is it just because males eat out in restaurants more often.

And one can objectively discriminate between those alternative causal hypotheses that being male is a direct driver of susceptibility versus being male is an indirect driver because it means you're more likely to have insurance coverage, eat out in restaurants and so forth.

So applying those standard techniques I was able to determine what was causal and what was not

within the ability of the data to resolve. And that's the basis for my published opinions and also for my testimony.

Q Now, if I recall correctly, Mr. Spiller asked if your opinion that the use of Baytril provides 25 more cases than it might caused was based on your model and I believe you said there is a much simpler way to get to these. What did you mean when you said that?

A I said it was based in part on my model but the basic facts -- the basic -- here's what's going on. If you use Baytril, you reduce the incidence of Erisycolitis in chicken flocks. Erisycolitis is a condition that leads to underweight chickens.

Underweight chickens, when they show up at processing plants, are out of tolerance for the machines there and they spray fecal matter here and there and the net result is the consumers see more microbial load coming at them.

Because I developed a model that tracks microbial loads on chickens I was able to quantify what is the expected health impact of the additional contamination that could be caused by the loss of

Baytril. So that was the -- that's the argument without the model. The model then adds number around that, and the essence of it is just to realize high microbial loads are the source of risk and Erisycolitis chickens have high microbial loads.

Q So you did not rely on A-17 for your opinion?

A No. A-17 was just an old -- that's just the starting point.

Q Dr. Cox, I don't want to mischaracterize Mr. Spiller's question, but if I were to sum it up, I would say that in terms of the questions Mr. Spiller has tried to question you and create the impression that you are the only one who has this opinion and that somehow your opinion is at odds with the community, and I believe yesterday he asked you about today's standards, could you please tell me whether you believe that your opinion is outside the mainstream on risk assessment in this issue?

MR. SPILLER: Object to the form of the question as it incorporates counsel's characterization. It sounds like the actual question may have been the last part.

JUDGE DAVIDSON: Sustained. Do you want to ask it again?

MR. NICHOLAS: I will, your Honor. Thank you.

JUDGE DAVIDSON: And I'm cautioning the witness not to repeat what you've already said on the record. I recall one of the first questions that was asked you. This is -- along the vein of this is Cox as opposed to the world and you explained that that wasn't the case, there are other people who hold it, so I don't want hear the same thing over again.

THE WITNESS: Got you. Thank you, your Honor.

BY MR. NICHOLAS:

Q Dr. Cox, do you believe your opinion is outside the mainstream of people who have looked at this issue and looked at risk assessment with respect to the question of whether the use of Baytril or antibiotics in veterinary medicine has an impact on human health?

A Being mindful of his Honor's direction, I'll answer that I believe the mainstream is becoming redefined. I think that five years ago and ten years ago, common knowledge in the mainstream -- common

belief was that chicken was the primary source.

Now I look at papers like Rosenquist's. I look at the Rodriguez paper and other papers from the United Kingdom, where I see a lot of support. People are saying it doesn't seem to be chickens, what could it be, why didn't things go down when we got rid of a drug.

So no, I don't think that my opinion is outside the changing paradigm of what would be mainstream.

Q I believe, as well, you were questioned about restaurant dining, and the question was whether it isn't the chicken in the restaurant that's causing campylobacteriosis.

Do you believe it's chicken in the restaurant that's causing campylobacteriosis?

A I like to derive all of my assertions off of data. In the data, I do not see evidence for that hypothesis, and I do see evidence against it. Also, once I've done my own analysis, I like to look at what other people have said and here, the Rodriguez and other papers explicitly address that issue and the big

thing is it doesn't look like it could be chickens because those same chickens, by and large, go home and people roll around in them, basically. I mean, there's chicken juice, raw chickens.

No, I don't -- based on that evidence and based on the literature, no, I don't think that it's really chickens that are doing it.

MR. NICHOLAS: Thank you. I have no further questions, your Honor.

JUDGE DAVIDSON: Recross?

MR. SPILLER: Yes, your Honor, very few.

RECROSS EXAMINATION

BY MR. SPILLER:

Q The last question might be freshest in your mind, Dr. Cox. I understand you don't believe it's chicken in the restaurant. Do you believe it's campylobacter in the restaurant?

A That --

Q Causes campylobacteriosis in the humans who dine there.

A Again, I hate to get out in front of the data but yes, campylobacteriosis causes campylobacter -- or

the other way around. Excuse me. Wrong way.

Q And apart from chicken, in this record, in your testimony, how do you suppose the campylobacter got into the restaurant?

A Did you say we could include all the stuff like drinking water -- I'm sorry -- ground water or streams contaminated, so forth?

JUDGE DAVIDSON: He just asked you what you got.

THE WITNESS: Thank you. First, I haven't found any useful data to study it, but water on lettuce, the hands of the restaurant workers, as we've seen in some outbreak studies, non-poultry meats and vegetables. If you go to a salad bar you'll find campylobacter.

The key question for me is always do you get enough of it to cause illness with high probability, and I think the consensus now is well, once in a while you do, whether it's people shedding, what it is I don't think can be unambiguously identified from the data, but it doesn't look like chicken is the primary or predominant source.

BY MR. SPILLER:

Q And you mentioned in that answer do you get enough of it. I believe on redirect you indicated it was the exceptionally high loads that are the ones that cause people to get sick.

A Disproportionately so, yes.

Q In this record, thinking of the one person who got the lowest known dose tested in this record, did he get sick?

A Are you referring to Robinson?

Q I'm referring to Dr. Robinson.

A The lowest reported infectious level of which I'm aware is Robinson's.

Q And did he get sick?

A He did.

Q Was that an exceptionally high dose?

A 500 CFUs, compared to what most people get? I think it's many times the average.

Q You mentioned also that you preferred to use a causal analysis and you have some causal anal -- I think you said causal graphic analysis --

A Causal graph analysis.

Q Causal graph analysis. Is that exemplified, for instance, in Exhibit G-1811 that you still have up there?

A Can you tell me which G-1811 it is?

Q That's the International Journal of Infectious Diseases.

A You know, I don't -- can you --

Q I think your counsel left the copy for you. He certainly asked you questions about it.

A Hold on. I'm getting buried here. Okay. I found the paper.

Q So if you look, for instance, at page 3S30 of that, is that a causal graph analysis?

A This is a -- you mean the figure, right?

Q I mean figure 3.

A Thank you. No. This is a classification tree that reveals what are called conditional independence relations. Conditional independence just means, look, if you see people going into restaurants and getting sick, is it because they went into the restaurants or is it because males go into restaurants and males get sick?

If going into restaurants is conditionally independent of getting sick, given that your male -- meaning males get sick at the same rate whether or not they go into restaurants, then we can say no, the data aren't really consistent with it being the restaurant.

So this kind of tree looks for conditional independence relations. It's very useful for saying are people getting excess days of diarrhea because of Fluoroquinolone resistance and the answer is very strongly no. But this would then get assembled into a causal graph model along the lines outlined in my book.

Q And these trees are grown using the commercial software that you described in your redirect, right?

A These trees were prepared using something called Knowledge Seeker which is commercial software. What I described in my redirect, I referred to SAS, S-Plus. The distinction between these is that the ideal form of analysis is the SAS analysis where you pour the data in, push a button, get the result.

In Knowledge Seeker, there's some flexibility about the order in which the factors are listed so there's -- it doesn't happen to be one of the ones that

I mentioned but it is a commercial package useful for getting at conditional independence relations as a prelude to causal analysis.

Q And referring to figure 4 in that paper, in this commercial software generated document, am I correct that in the grid analysis there the multiple question marks mean missing data?

A Missing data, no answer, yes.

Q Was it the machine or you who determined at each level of the classification whether to put the unsures or the no answers with the yeses or the nos?

A The machine.

Q And sometimes the machine puts the unsures with the yeses and sometimes it puts the no answers with the nos?

A That's correct. It tries to ask the most informative questions at each stage. Oh. And a key correction to the testimony I just gave is that at the bottom level of these trees, on the right-hand side you see there's a variable called eight chick. This is a reanalysis of the Smith, et al data set. Eight chick, as explained in the text, does not enter into the tree

by itself.

What that means is there's no statistical association between recently eating chicken and Fluoroquinolone resistance. Therefore, I forced that variable in and that would be an exception. I said no, yes and other. That was my choice, not the machine's choice.

Q So you can force this classification tree analysis.

A You can force -- you can split on a variable. You can't force non-significant variables to come into the tree analysis but you can take any one variable.

Q And in your figure 3 in that paper, the very top item, the first branch in the classification tree is Vis Farm, that's for whether or not the person visited a farm?

A I think recent farm visit was the longer name of that variable, yes.

Q And is the reason that that variable came off first because you got a very strong signal between the cases and controls, 99 and a half percent versus a half a percent?

A Let's see. Why this came out -- the answer may be yes but the salient point is I let these identified risk factors take themselves out of the analysis. They all showed up as lick and splits. I didn't want to analyze cases where we thought we knew what the explanation was going to be.

So as explained in more detail in the article, you'll see we take out foreign travel. I took out pet 08, which is having a puppy. Drinking boiled water. And this gets us down to sex. Not the end of the tree but the beginning of the expanded tree.

Now we get into stuff that I'm not just taking out. So, for example, if sex is really relevant, it makes a difference between 44 percent and the -- this is now autodiscovery, if you will.

Q And confining your answer, if you will, to my question, in the top classification, vis farm, you got a very strong signal between the cases in the controls there. They split 99 and a half percent one way and a half a percent the other, didn't you?

A On the right-most branch.

Q Yes.

A Yes.

Q And tell the record why we pulled out 211 cases for that.

A For two reasons. The first I've alluded to, which is I didn't want to look at things where visiting a farm or foreign travel, both of these might be the issue. And secondly, because we didn't have data on those people. 7 is the code for not applicable or didn't answer. Question mark is the default code for missing data.

Q Did it not seem remarkable to you as a professional analyst of data that not having data would so strongly be correlated with the distinction between cases and controls? Why would cases versus controls be lacking data?

A Oh. This gets back to the fact that it's survey data. You have a bunch of recall biases, people are more willing to think about 101 chicken questions under some conditions, like they're -- you plant the idea it's chicken that's the problem, they may be more willing to put up with a long questionnaire. And I see this kind of thing in data from telephone companies and

-- it's not all initial.

Q Do you know, Dr. Cox, whether that elimination was actually based on whether they were a secondary or a primary case in the family?

A No.

Q So you don't actually know why your commercial software no human hands-on classification tree lost out on 211 of the data points in the study?

A Well, I know that I sent out the visit farm cases or allowed to select themselves out -- the visit farm cases and I stuck with the 1,104 who said no, I've not visited a farm. I'm trying to eliminate competing explanations.

Q Dr. Cox, you mentioned on redirect your recent model was not yet published, it was in the peer review process?

A That's correct.

Q And I think you mentioned that one of those papers that's in review was currently -- had won you a best paper award from SRA.

A Yes, it did.

Q Congratulations.

A Thank you.

Q What peer review process is involved in the choice of who gets the best paper award at the Society for Risk Analysis?

A I don't know the details. The chair of the committee is also the president of the Society and there's a ladder where you start off just submitting abstracts, maybe 600, a thousand -- some large number of abstracts are submitted. And then the committee says well, this looks interesting. Can you draft three or five pages, which is kind of the second round.

And based on those so-called extended abstracts, you may then be invited to submit a whole paper. That's the -- now you're getting close to the end of the process.

Then those who are I believe officers of the Society -- the high and mighty of the Society for Risk Analysis then ultimately winnow down perhaps 350 fully developed abstracts to last year 7 finalists and then they notify you of that.

Personally I wouldn't consider that a peer review. I mean, yeah, your peers look at it, but

that's the prelude to then submission and peer review. So that's what I know of the process.

Q Thank you, and I appreciate the answer there at the end.

MR. SPILLER: Your Honor, I have no further questions on recess.

JUDGE DAVIDSON: Mr. Nicholas, do you need anything else?

MR. NICHOLAS: No further questions, your Honor.

JUDGE DAVIDSON: You're excused, Dr. Cox.

THE WITNESS: Thank you.

(The witness was excused.)

JUDGE DAVIDSON: Ms. Steinberg, what have you got for me?

MS. STEINBERG: Yes, your Honor. During the lunch break I did look at the documents that you asked about and I do have an answer. I believe that all the documents are different. The one that might be the same is G-1806 and B-1946. For clarity I would ask that all of this be put in the record and marked with exhibit numbers.

JUDGE DAVIDSON: Okay. I had asked Ms. Steinberg to check because my records show that 1806, 1807, and 1808 that I had ruled out and then when you put in 1946 and 47, I let them in. I figured it should all be in or it should all be out. I didn't think that -- because they're somewhat the same, they're slightly different.

They all deal with the same issue. I didn't think it qualified as evidence, to tell you the truth. I think they should all be out. But you moved 1946 and 47 into the record to offset stuff that I didn't put into the evidentiary record. This is dealing with his qualifications, with his degrees, with the letters from the --

MR. NICHOLAS: Your Honor --

JUDGE DAVIDSON: I understand what happened. It's not your fault. So I still say I'd just as soon not have them in but if you want them in, I'll leave them all in.

MR. NICHOLAS: We're happy to just withdraw those.

JUDGE DAVIDSON: Okay. So none of them will

be in the evidentiary record.

(Respondent Exhibits 1946 and 1947 were withdrawn.)

JUDGE DAVIDSON: Now, we have 1936. I don't think I've ruled on that. B-1936. Looks like a one-page document dealing with PubMed Chemotherapy Agents campylobacter.

MR. NICHOLAS: That's the Hollander article, your Honor. It's an abstract with respect to --

JUDGE DAVIDSON: Right. Abstract. I just want to clean up my paper here.

MR. SPILLER: Could we see it, your Honor? In our confusion, we don't have a collective recollection of what it is.

JUDGE DAVIDSON: You don't remember it?

MS. STEINBERG: No objection, your Honor.

JUDGE DAVIDSON: Okay. B-1936 is received.

(Respondent Exhibit 1936 was marked for identification and received in evidence.)

JUDGE DAVIDSON: Now, I have G-1809, 1811, 1816 and 1817, which were introduced by the CVM during

the cross-examination of Dr. Cox.

I don't even think -- I don't know if you moved them into evidence or you just want to leave them there.

It's okay with me, whatever you choose.

MR. SPILLER: Your Honor, 1811 is the International Journal of Infectious Diseases and if I did not previously make explicit, we do not need this as an exhibit, your Honor. If it can be subject to discussion, that's fine. If counsel needs it for clarification --

MR. NICHOLAS: Your Honor, we would like to have that in the record, provided we could use the full-blown report. I believe parts of this report are already in the record, your Honor, but since the issue --

JUDGE DAVIDSON: Well, we handled the page with the names on it already. He read the ones in the record.

Is there something else in there you think is missing?

MR. NICHOLAS: I believe all the rest of the

papers that are discussed in here are in the record, your Honor.

I don't believe there are discussions with respect to --

JUDGE DAVIDSON: I'm sorry; what discussion?

MR. NICHOLAS: These are the proceedings that --

JUDGE DAVIDSON: I understand what they are --

MR. NICHOLAS: And the proceedings contained both authored papers as well as discussion.

JUDGE DAVIDSON: And the discussions, you say, are not here?

MR. NICHOLAS: I don't believe so, your Honor.

JUDGE DAVIDSON: I'm not trying to say you're wrong, but there's a section entitled "discussion." Is that not the same thing?

Well, it won't be received in evidence and if you think it's important to get the whole thing in, you can try again. But as I said before, it's got to end sometime. So 1911 is not received in evidence. Excuse me, G-1811.

MR. SPILLER: And your Honor, G-1816 is the

Robinson study. If I did not previously, I now move G-1816 in evidence.

JUDGE DAVIDSON: Any objection?

MR. NICHOLAS: No, your Honor.

JUDGE DAVIDSON: It's received in evidence, 1816.

(Government Exhibit 1816 was marked for identification and received in evidence.)

JUDGE DAVIDSON: Now 1817.

MR. SPILLER: 1817 is a copy of a portion of a Rosner textbook and includes the disputed definition of the central limit theorem, I believe, and if I did not previously, I do now move 1817 in evidence.

MR. NICHOLAS: We have no objection, your Honor.

JUDGE DAVIDSON: All right. 1817 is received in evidence.

(Government Exhibit 1817 was marked for identification and received in evidence.)

MR. SPILLER: Your Honor, I believe the last

one on the list is G-1809, which is the collection of e-mail correspondence between the witness, Dr. Cox, and Mr. David Vose, which has been discussed at several points both in cross and on redirect. And if I did not previously, I do now move that exhibit in evidence.

MR. NICHOLAS: We have no objection.

JUDGE DAVIDSON: Okay. It's received in evidence.

(Government Exhibit 1809 was received in evidence.)

JUDGE DAVIDSON: Any others I missed? I hope not.

MR. NICHOLAS: No, your Honor.

JUDGE DAVIDSON: Okay. You can sit down, Dr. Cox. Find a chair.

Okay. I think we're finished. We just have to take care of some minor things like transcripts. Does anybody know how long it's going to take to get the transcript?

THE COURT REPORTER: I don't know.

JUDGE DAVIDSON: Okay. I just wanted to know if either of the parties had contacted your agency to

determine what the normal time is. No?

MS. STEINBERG: We don't know, your Honor.

JUDGE DAVIDSON: How about a date for briefs? First of all, don't make it too long, because I'm going to limit them, and the first limitation I'm putting in is -- as I said, I can't tell you how to organize it but I would appreciate it if you would organize your briefs in such a manner as to A, follow along with the issues in this proceeding. That is, you start with whether or not the Agency has met its threshold obligation of requiring the burden going forward to shift to the manufacturer to prove safety and efficacy.

And that, I think, is well-documented in our previous motions and discussions and things, the fact that there is a threshold burden on the Agency doesn't necessarily constitute, quote, unquote, new evidence, but it does include a look at the evidence, a new look at the evidence which justifies a finding that the prior finding is no longer valid and therefore the burden of going forward would shift to the manufacturer.

So that's the first issue I'd like you to

discuss.

After that, I'd like you to organize your briefs in such a way as to deal specifically, if we get to that, and in Bayer's point I guess that would be in the alternative, dealing with the rest of the evidence and the proceedings in line with the issues as presented in the NOH.

Now, I want you to do all that in 10 pages. I would like you to do it in as few pages as possible, but I will admit for the record that I don't claim to be a statistician, I don't claim to be a scientist, so I'm going to need you to refer to the evidence, not your own ideas of what this is, but what the evidence shows, in a way that witnesses have supposedly explained all this and in simplified terms to me.

It's not you explaining it to me; it's the witnesses having explained it to me in their testimony or in the transcript. And back to the old simplify, simplify. That's what I need. If you want me to read your conclusion in a reasonable amount of time, I've got to understand what I'm doing.

So far I think I'm sticking with it pretty

good, but a lot of the technical stuff I want you to point to where the witnesses have made it clear, because that's why they're witnesses, in order to explain to the so-called novice what they're talking about.

Along those lines, I do not expect you to reproduce testimony in your brief. I do not expect you to reproduce things that are already in the record; references would be sufficient. But I caution you that they have to be accurate and the citations have to reflect what they're cited for, otherwise I'm going to just throw them out.

Okay. I've wrestled with the idea -- I usually have concurrent briefs, but because of my admission, my own lack of statistical expertise and scientific expertise, I'm thinking that I might allow reply briefs.

They'd still be concurrent, but an opportunity to reply, which even means that maybe it will be five pages initially instead of ten.

Anybody have any thoughts on that pro, con, or otherwise with respect to the concurrent reply briefs?

MS. STEINBERG: CVM is in favor of that.

MR. NICHOLAS: Bayer is in favor of that, your Honor.

JUDGE DAVIDSON: All right. How about 100 pages initially, 50 pages in reply? And I've got to be able to read it, so don't give me this tiny little print just so you can get it into a hundred pages.

Okay. Due date. I'll take your suggestions and then I'll rule. And we'll allow two weeks for the transcript to be completed. You can go from there. Anybody care to venture a stab?

MR. NICHOLAS: I was going to suggest, your Honor, that we confer with CVM and then get back to you tomorrow morning on that, if that's acceptable?

MS. STEINBERG: Your Honor --

JUDGE DAVIDSON: Yeah.

MS. STEINBERG: Instead of waiting until tomorrow, would it make sense for us to confer in the next few minutes?

JUDGE DAVIDSON: If you think you can. I want to tell you, you know, I don't give -- I'm not talking two, three months here.

If you can come up with something reasonable within that time frame, including the replies, maybe it will be all right.

I'll go off the record and you sit down and talk and come back with your proposal for briefs and reply briefs. I have a calendar here so I should be able to make sure that you're not required to file anything on a Saturday or Sunday. I won't guarantee the holidays.

Off the record.

(A discussion was held off the record.)

MS. STEINBERG: Your Honor, during the recess, counsel for Bayer and counsel for CVM conferred and we have a joint proposal for due dates. We propose that the initial brief be due July 18 and that the reply briefs be due August 15.

JUDGE DAVIDSON: July 18 is my anniversary. I'll be married 45 years on July 18.

MR. NICHOLAS: The 19th?

JUDGE DAVIDSON: That will be the Saturday.

MR. NICHOLAS: A present on the 18th.

JUDGE DAVIDSON: Oh, God, no.

MR. NICHOLAS: Your wife would kill us.

JUDGE DAVIDSON: All right. July 18. I knew there was something familiar about that. Two months. You better do a decent job, I'm giving you so much time.

MR. NICHOLAS: You've given us such a challenge, your Honor, we need it.

JUDGE DAVIDSON: And the response you said was August?

MS. STEINBERG: August 15.

JUDGE DAVIDSON: Done.

MR. NICHOLAS: Thank you, your Honor.

MS. STEINBERG: Thank you, your Honor.

MR. SPILLER: Thank you, your Honor.

JUDGE DAVIDSON: Now remember what I said about -- I'd just as soon not have any more evidence come in unless it really qualifies as, quote, new evidence, because administrative proceedings, that's always acceptable if something new really comes in that is of that kind of merit that requires, in effect, reopening the proceeding.

Otherwise, we are adjourned.

MR. SPILLER: Thank you, your Honor.

MR. NICHOLAS: Thank you, your Honor.

MS. STEINBERG: Thank you, your Honor.

(Whereupon, at 3:10 p.m., the hearing was concluded.)

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